# PMPRB Steering Committee on Modernization of Price Review Process Guidelines

Final Report
July 2, 2019

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# 1. Purpose

The purpose of this report is to summarize the deliberations of the PMPRB's Steering Committee on Modernization of Price Review Process Guidelines (the "Steering Committee") in providing stakeholder feedback on the Patented Medicine Prices Review Board's ("PMPRB") proposed new framework for regulating the prices of patented medicines. The report has been prepared by PMPRB staff and will be shared with the Board for its consideration prior to the publication of new draft guidelines for public consultation later this year.

# 2. Introduction

The PMPRB is consulting with its stakeholders on changes to its non-binding guidelines (the "Guidelines"), as contemplated by subsection 96(4) of the Patent Act. The purpose of these changes is to modernize the PMPRB's approach to carrying out its mandate to protect Canadian consumers from excessive patented medicine prices. Two main types of changes are contemplated. The first type would operationalize Health Canada's proposed amendments to the *Patented Medicines Regulations* in order to make patented medicines more affordable for Canadians. The second would enable the PMPRB to make more efficient use of its resources by adopting a risk-based approach to how it regulates.

The mandate of the Steering Committee is to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of new draft Guidelines that would give effect to these changes. This work was based in part on the analysis and recommendations of a technical Working Group (the "Working Group") with expertise in health technology assessment and other economic and scientific matters.

Any analysis or recommendations resulting from the Working Group's review or from the Steering Committee's deliberations will be carefully considered by the Board prior to the release of new draft Guidelines but are not binding on the Board or PMPRB staff.

## 2.1. Membership

The Steering Committee was jointly chaired by Tanya Potashnik, the PMPRB's Director of Policy and Economic Analysis and Matthew Kellison, the PMPRB's Director of Regulatory Affairs and Outreach. The Steering Committee consisted of 15 members from the stakeholder community and included observers from Health Canada and Innovation, Science and Economic Development (ISED). PMPRB officials attended meetings to provide administrative and other support, as required. Members and observers are identified below.

| Name | Title |
|---|---|
| Suzanne McGurn | Assistant Deputy Minister, Ontario Public Drug Programs Division, Ontario Ministry of Health and Long Term Care<br>Member - Jurisdictional (Ontario) and Vice-Chair of the Board, CADTH |
| Mitch Moneo | Assistant Deputy Minister, Pharmaceutical Services Division, Ministry of Health, British Columbia<br>Member - Jurisdictional (Western Provinces), CADTH |

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| Scott Doidge<br>(Alternate: Susan Pierce) | Manager, Pharmacy Policy Development Division, Department of Indigenous Service Canada |
| Dr. Robin McLeod (Alternate: Michael Sherar) | VP, Clinical Programs and Quality Initiatives, Cancer Care Ontario |
| Brian O'Rourke<br>(Alternates: Heather Logan, Brent Fraser) | President and Chief Executive Officer, Canadian Agency for Drugs and Technologies in Health (CADTH) |
| Dr. Luc Boileau<br>(Alternates: Sylvie Bouchard, Patrick Dufort) | President and Chief Executive Officer, Institut national d'excellence en santé et en services Sociaux (INESSS) |
| Stephen Frank (Alternate: Karen Voin) | President and CEO, Canadian Life and Health Insurance Association (CLHIA) |
| Pamela Fralick | President, Innovative Medicines Canada (IMC) |
| Laurene Redding | Director Pricing, Contracting and Negotiations AstraZeneca, BIOTECanada |
| Durhane Wong-Rieger | President and CEO, Canadian Organization for Rare Disorders (CORD) |
| Dr. Jeff Blackmer<br>(Alternate: Owen Adams) | Vice-President, Medical Professionalism, Canadian Medical Association (CMA) |
| Glen Doucet<br>(Alternate: Joelle Walker) | Interim CEO, Canadian Pharmacists Association |
| Gail Attara<br>(Alternate: Paulette Eddy) | President and CEO of the Gastrointestinal Society, Best Medicines Coalition |
| Martine Elias | Executive Director, Myeloma Canada |
| Jim Keon<br>(Alternate: Jody Cox) | President, Canadian Generic Pharmaceutical Association (CGPA) and President Biosimilars Canada<br>Vice President Federal and International Affairs, CGPA |
| Observers | Title |
| Karen Reynolds | Executive Director, Office of Pharmaceuticals & Management Strategies, Health Canada |
| Eric Dagenais | Assistant Deputy Minister, Innovation, Science and Economic Development Canada |
| Imran Ali | Senior Manager, pan-Canadian Pharmaceutical Alliance Office (pCPA) |
| Rodrigo Arancibia (Alternate: Benoit Leduc) | Deputy Director, Life Science Industries, Innovation, Science and Economic Development Canada |
| Declan Hamill | Vice-President, Legal, Regulatory Affairs and Compliance, Innovative Medicines Canada (IMC) |
| Paul Petrelli | General Manager, Jazz Pharmaceuticals |

## 2.2. Governance

Steering Committee members represent organizations with competing points of view on the policy rationale for the proposed amendments to the *Patented Medicines Regulations* upon which the

proposed framework changes are partly based. This was expressly acknowledged in the Steering Committee's Terms of Reference. As the regulator responsible for giving effect to these amendments, the PMPRB's role is to conceive a Guidelines framework that is fair, functionally sound and rationally connected to the nature and scope of Health Canada's proposed policy. Members were encouraged to work constructively with the Steering Committee to help the PMPRB fulfill its responsibilities in this regard, irrespective of their views on the underlying policy.

During the Steering Committee's tenure, the proposed amendments to the *Patented Medicines Regulations* had not been approved for final publication in Part II of the Canada Gazette. As a result, some members expressed the view that any discussion about the operationalization of the amendments was premature and that, in positing passage of the amendments in their currently proposed form, the proposed Guidelines framework was too narrow. PMPRB officials reiterated that comments or concerns about the proposed amendments were outside the scope of the Steering Committee's mandate but would be included in the appendices to this report.

The Terms of Reference were reviewed by all members. IMC requested that the record reflect its opposition to the proposed amendments to the *Patented Medicines Regulations,* notwithstanding its participation in the Steering Committee.

## 2.3. Procedure and Process

The Steering Committee held three face-to-face meetings in Ottawa on June 25, 2018, December 13, 2018, and May 13, 2019, as well as four teleconferences on July 24, 2018, August 15, 2018, September 12, 2018 and March 15, 2019. Meeting presentations and summaries prepared by Board Staff are included in the Appendix to this report.

At the first meeting, the co-chairs presented an outline of a new proposed five-part Guidelines framework to members. Subsequent meetings were spent discussing each of these parts in greater detail, with members exchanging ideas and seeking clarifications from Board officials. In general, members representing patient groups were concerned about the potential impact of the changes on continued access to medicines, clinical trials and patient support programs. Members representing the pharmaceutical industry generally expressed concerns that the proposed framework could introduce uncertainty with respect to the price of a medicine in Canada and thereby impact the decision of whether to bring it to market. Conversely, members representing payers generally expressed the view that the proposed changes would provide much needed collaborative federal support to manage the challenges posed by high drug prices.

Members were asked to provide written feedback on specific questions relating to each part of the proposed framework by April 8, 2019. All written feedback is included in Section 8 of this report, including feedback that is outside the scope of the Terms of Reference.

Steering Committee members representing BIOTECanada requested that specialized groups be struck to examine certain operational matters not before the Technical Working Group. However, it was the view of the co-chairs that the matters identified were not sufficiently high level to warrant elucidation at this stage in the consultative process.

Throughout the Steering Committee's deliberations, PMPRB officials provided regular updates on the parallel progress of the Working Group. On March 15, 2019, the Chair of the Working Group

summarized its findings to the Steering Committee by webcast. The Chair also attended the final Steering Committee meeting on May 13, 2019, to present the report in greater detail and answer technical questions from the Steering Committee on its content.

PMPRB officials presented case studies to the Steering Committee at the December 13, 2018 meeting to illustrate how the PMPRB's current approach to regulating prices would change under the proposed framework.

On March 20, 2019, a questionnaire soliciting final written feedback was sent to the Steering Committee members. At that time members were also asked to identify any additional questions they had regarding the final report of the Working Group.

The draft Steering Committee report was sent to members on May 7, 2019 and discussed at its meeting on May 13, 2019. Steering Committee members were given the opportunity to review the draft and provide feedback prior to the publication of the final report.

# 3. PMPRB Framework Modernization

The co-chairs presented an outline of the proposed five-part Guidelines framework to the Steering Committee on June 25, 2018 (See Appendix 9.2), which is summarized below.

## 3.1. Part 1: MLP based on MIPC

Part 1 envisions a 'Maximum List Price' (MLP) for all new medicines at introduction. The MLP would be a transparent ceiling price based on public list prices net of any rebates. The initial MLP would be based on the median international prices of the PMPRB12 (MIPC). The MLP would be interim until the medicine is sold in seven countries or has been sold in Canada for three years, whichever comes first. Following this it would be fixed and the prices of the medicine could vary freely below this level in subsequent reporting periods.

## 3.2. Part II: Categorization

Medicines would be screened as either high priority (Category 1) or low priority (Category 2) based on the anticipated impact on Canadian consumers, including individual patients and institutional payers. Four screening criteria were proposed:

1. The medicine is first in class or a substantial improvement over existing therapy[1];
2. Expected sales exceed the affordability threshold of $20 million annually[2];
3. The opportunity cost of any clinically significant indication of the medicine is greater than $30,000/quality-adjusted life year (QALY);[3] and/or
4. The average annual treatment[4] cost is above per capita GDP.

[1] This was later refined to specify "first in class or a substantial improvement over existing medicines for clinically significant indication(s)"in the August 15, 2018 presentation.
[2] This preliminary threshold was left unspecified in the August 15, 2018 presentation.
[3] This preliminary threshold was left unspecified in the August 15, 2018 presentation.
[4] This was expanded to include "course of treatment cost" in the August 15, 2018 presentation.

### 3.3. Part III: Category 1: MRP

Category 1 medicines would have both a MLP, which would be public, and a 'Maximum Rebated Price' (MRP), which would be known only to the patentee. The MRP would be assessed against net (after rebate) prices and determined in a two-step process for Category 1 medicines based on pharmacoeconomic, market size and GDP factors.

In the first step, the cost-effectiveness of Category 1 medicines would be considered by applying a pharmacoeconomic factor. Patentees would be required to provide the PMPRB with all published cost-utility analyses that express value in terms of the cost per QALY. All Category 1 medicines would be subject to a maximum cost effectiveness threshold of $60,000/QALY, although certain clinical characteristics (*e.g.*, a high burden or disease or significant absolute gain in QALY) could warrant a higher absolute ceiling price.

The MRP could be further adjusted following the application of the pharmacoeconomic factor if there were affordability concerns based on the prevalence of the indication the medicine is expected to treat. In the second step, the MRP of Category 1 medicines that have a market size exceeding $20M[5] per year would be subject to a percentage reduction that increases with expected market size. An initial market size threshold of $20M per new medicine is proposed based on the contribution of new medicines to GDP and GDP growth from 2012 to 2017.[6] This threshold would change annually depending on GDP growth.

The MRP would be fixed at introduction and the price of the medicine could vary freely below this level in subsequent years without triggering further review (except in the case of re-benching discussed below).

### 3.4. Part IV: Category 2: MLP

The final MLP for Category 2 medicines would be set the lower of the MIPC and the average of the domestic therapeutic class (TCC).[7] Category 2 medicines will only have an MLP and no Category 2 medicine will have an MLP that is lower than the lowest price in the PMPRB12 (LIPC).

### 3.5. Part V: Re-benching

The framework contemplates possible adjustments to the MLP and MRP after introduction (*i.e.*, "re-benching) in response to specific changes in market conditions such as:

1. Approval of a new indication;
2. Actual revenues that diverge significantly from those forecasted at introduction;

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[5] A preliminary figure of $40M was used for modelling purposes in the "Proposed Application of PE and Market Size Factors to Category 1 Drugs" case study provided to Steering Committee members on December 13, 2018.

[6] The calculation to estimate an affordability market size threshold is based on growth in the Canadian GDP over a defined period that identifies the market size for each medicine that would be associated with keeping the share of expenditures on medicines constant relative to expenditures on health. Medicines that exceed that amount are expected to account for a higher relative share of overall expenditures than what would be "absorbable" by the growth in GDP at the individual medicine level.

[7] The TCC could also be used in establishing the MLP of Category 1 medicines. This concept was first provided to Steering Committee members in the "Proposed Application of PE and Market Size Factors to Category 1 Drugs" on December 13, 2018.

3. New evidence on cost-effectiveness (*e.g.*, a CADTH/INESSS therapeutic class review or the lifting of Health Canada conditions for a Notice of Compliance); and/or
4. Significant changes in prices in the PMPRB12 comparator countries (*e.g.*, the MIPC exceeds the MIPC at introduction by more than 25%).

Patentees could also seek to have their medicines re-benched if there is evidence of improved cost-effectiveness, smaller than expected market size, or a significant increase in CPI.

### 3.6. Price review by class of customer

Price reviews would be conducted for three customer classes based on patentee filings. All medicines would have be assessed against the MLP, with assessment against an MRP reserved for Category 1 medicines only:

1. National Retail: The list prices of all medicines would be reported and assessed against the MLP.
2. National Private Payer: Sales to private payers will be reported at the national level. The national average transaction price (ATP) of all sales reported to private payers will be assessed against the MRP. The ATPs are calculated net of all direct and indirect benefits and discounts.[8]
3. Provincial Public Payer: Sales to public payers will be reported at the provincial/territorial level. The ATP in each province/territory, net of all discounts, will be assessed against the MRP.

Complaints would trigger an investigation into whether the price of medicine is consistent with the Guidelines and whether market conditions have changed following the original assessment such that a re-benching and/or re-classification is warranted.

### 3.7. Application of new Guidelines to existing medicines

Medicines being sold in Canada prior to the implementation of the new framework ("existing medicines") would be given an interim price ceiling based on the MIPC of the PMPRB12[9]. If the cost of any indication exceeds $100,000/QALY, the medicine would be classified as Category 1 and prioritized for re-benching. All other existing medicines would be considered Category 2 and re-benched at a later date, with all medicines within a therapeutic class being re-benched at the same time. Re-benching of Category 2 medicines could be prioritized if a complaint is received.

Patentees whose medicines are slated for re-benching would be advised in advance and, if a price reduction is warranted, given two reporting periods to respond accordingly.

## 4. Topics for Discussion

Over the course of their deliberations, Steering Committee members discussed several topics, as summarized below.

[8] This concept was expanded to include "all direct and indirect discount and benefits" in the September 12, 2018 presentation.

[9] The approach was further refined in the September 12, 2018 meeting to "Existing medicines would be given an interim ceiling price based on the lower of their current ceiling and the MIPC of the PMPRB12".

### 4.1. Use of External Price Referencing (EPR) in Part 1: Median International Price Test (MIPC)

PMPRB officials presented the proposed use of EPR:

- All new medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).
- This MIPC would be interim until the medicine is sold in seven countries or three years post first date of sale.
- The MLP could be re-benched over time.

Members were asked the following questions:

1. Is an MLP based on the median of PMPRB12 (MIPC) for all medicines reasonable?
2. Should exceptions be made to the MLP-MIPC test and, if so, when and why?
3. Should there be a price floor for Category 2 medicines based on Lowest International Price (LIPC)?
4. Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?
5. Should an increasing gap between the MIPC and the MLP trigger a re-bench?
6. Should EPR differ depending on the category or vintage of the patented medicine?

### 4.2. Use of List Price and Net Price Ceilings (MLP, MRP)

PMPRB officials reviewed the proposed framework previously presented to the Steering Committee.

- Category 1 medicines would have two ceilings: one based on list price (MLP) and one based on net (rebated) price (MRP).
- Category 2 medicines would have one ceiling price (MLP) based on the lower of the average domestic Therapeutic Class Comparison test and the MIPC test. No Category 2 medicine would have an MLP that is lower than the lowest country in the PMPRB12.

Members were asked the following questions:

1. Should a Category 1 medicine ever have more than one MRP?
2. Are there economic considerations that would support a higher MRP for some Category 1 medicines that would result from the proposed application of the new factors?
3. Should confidential third party pricing information only be used for compliance purposes?

### 4.3. Risk Assessment and Prioritization Criteria for Category 1 and 2 Medicines

PMPRB officials reviewed the proposed classification criteria previously presented to the Steering Committee.

- New medicines would be categorised as Category 1 or 2 based on their anticipated impact to Canadian consumers.
- Categorization criteria would take into consideration:
    - Therapeutic alternatives
    - Market size
    - Opportunity cost
    - Annual/treatment cost

- Category 1 medicines would be subject to a comprehensive review to determine if the price is excessive.

The PMPRB shared analysis that models the impact of using different threshold parameters for each of the categorisation criteria.

Members were asked the following questions:

1. Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?
2. Should further categories exist with differential treatment modalities?
3. Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?
4. Should the pharmacoeconomic, market size and GDP factors apply as both screens and thresholds?
5. Should Category 2 medicines be scrutinized more or less than proposed?

### 4.4. Re-benching Criteria

PMPRB officials reviewed the proposed re-benching criteria previously presented to the Steering Committee.

- Approval of a new indication
- Sales in excess of expected market size
- New evidence of cost effectiveness
- Significant changes to international prices
- Application by the patentee for a re-bench with evidence of increased cost effectiveness, smaller market, or a significant increase in CPI

Members were asked the following questions:

1. How often and in what circumstances should a medicine be re-benched?

### 4.5. Tests for Category 1 Medicines

PMPRB officials presented the following tests for Category 1 medicines:

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).
- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

Members were asked the following questions:

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?
2. Should exceptions be made to the MIPC test and, if so, when and why?
3. Should the cost effectiveness threshold for Category 1 medicines vary?
4. Should a Category 1 medicine ever have more than one MRP?
5. Are there economic considerations that would support a higher MRP for some Category 1

medicines than would result from the proposed application of the new factors?

## 4.6. Tests for Category 2 Medicines

PMPRB officials reviewed the proposed tests for Category 2 medicines.

- Category 2 medicines would have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class.
- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex-factory) prices, domestically and internationally.

Members were asked the following questions:

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?
1. Should exceptions be made to the MIPC test and, if so, when and why?
2. Should there be a price floor for Category 2 medicines and, if so, should it be based on LIPC?
3. Should Category 2 medicines be scrutinized more or less than proposed?

## 4.7. Use of Confidential Pricing Information

PMPRB officials reviewed the proposed ways in which confidential pricing information may be considered.

- Price reviews would be conducted for the following customer classes:
    a. National/Provincial Retail – list price assessed against MLP
    b. National Private Payer – ATP assessed against MRP
    c. Provincial Public Payer – ATP assessed against MRP in each market
- ATPs would be calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

Members were asked the following questions:

1. Are the proposed definitions of markets and customer classes reasonable?
2. Is the proposal to use third-party pricing information for compliance with the MRP reasonable?
3. Other questions proposed by Steering Committee members?

## 4.8. Application of New Regime to Existing Medicines

PMPRB officials reviewed the proposed method of applying new Guidelines to existing medicines.

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 medicines would be re-benched later unless a complaint is received.

- All medicines within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to address the issue.

Members were asked the following questions:

1. Is the use of MIPC as an interim ceiling reasonable?
2. Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?
3. Are there reasonable alternative approaches to bringing existing medicines under the new framework?
4. Other questions proposed by Steering Committee members?

### 4.9. Additional Questions for Consideration

The following additional questions were put to Steering Committee members for their consideration:

1. Are there opportunities to further reduce regulatory burden while still operationalizing the new factors?
2. Are there other questions proposed by Steering Committee members?

## 5. Feedback

All the written feedback received during this process was shared with all Steering Committee members and is included in section 8 of this report. Given that not all Steering Committee members responded to the questions posed on the proposed framework, it was not possible to identify common points of agreement. Some members indicated they did not feel informed enough to meaningfully respond in writing, given the technical nature of some of the topics posed to the Steering Committee.

Steering Committee deliberations were summarized by PMPRB officials and circulated to Steering Committee members for review and comment subsequent to each meeting. These summaries are in section 9.3 of the Appendix to this report.

Steering Committee members agreed that PMPRB officials would summarize any questions that arose over the course of each meeting and provide members with an opportunity to provide relevant written feedback afterward. The deadline to provide that feedback was three working days before the next such meeting so that officials would have sufficient time to prepare a response if warranted.

As their deliberations unfolded, some members expressed concern, both verbally and in writing, that the framework presented to them by PMPRB officials was in such an advanced state of design that it left little room for a discussion of possible alternative approaches. PMPRB officials sought to assure the Steering Committee that alternative approaches to operationalizing the proposed regulatory amendments were welcome, but that the framework reflected the agency's best efforts to provide stakeholders with the level of detail necessary to understand the full import of the policy behind the amendments. At the Steering Committee's meeting of December 13, 2018, the PMPRB's Chairperson further observed that it would not have been fair or realistic to put the onus of conceiving the framework from a more embryonic state on stakeholders given their competing views on the merits of the underlying policy.

Steering Committee members were asked to provide final written feedback to the questions identified by the PMPRB over the course of deliberations by April 8, 2019.

Written responses to these questions and earlier requests for feedback were received from CORD and Myeloma Canada, the CMA, the BC Ministry of Health, BMC, BIOTECanada, IMC and CHLIA.

Discussion and feedback from the Steering Committee also resulted in changes to the proposed framework over the course of the Steering Committee's work. For example, the proposed screening criteria and thresholds used to classify a medicine as Category 1 or Category 2 have evolved, as noted in Section 3 of this report. Additionally, technical issues that warrant subsequent working groups, such as tracing ex-factory sales to the end user in order to provide the PMPRB with a medicine-level breakdown of specific benefits given to public or private payers, were identified for subsequent consultations.

## 6. Summary of Working Group Recommendations

In July 2018, the Technical Working Group was established to provide expert insight and advice to the Steering Committee on certain economic and scientific matters relating to the new framework.

The Working Group's Terms of Reference directed it to examine and make recommendations with respect to specific considerations and questions within the following six 'areas of focus':

1. Criteria for classifying medicines as 'Category 1'
2. Supply-side cost effectiveness thresholds
3. Multiple indications
4. Accounting for uncertainty
5. Perspective
6. Market size factor

The Working Group's final report was provided to the Steering Committee on March 15, 2019 and the Chair of the Working Group briefed the members on the report personally at their final meeting on May 13, 2019. A presentation summarizing the Working Group's report is included in the Appendix to this report. More information on the Working Group's activities, including its membership, process and procedure, a summary of deliberations, and 'on the record' comments from members, can be found in its final report, included in the Appendix of this report.

## 7. Final Report and Next Steps

PMPRB officials presented a draft of this report to the Steering Committee on May 13, 2019. In addition to discussing the draft and reiterating their feedback, members discussed the importance of developing a flexible system that is adaptable to future challenges in an environment where medicines are increasingly individualized. Further, members recommended the need to implement a change management plan to evaluate the success of the new regulatory framework going forward and to adjust the framework based on real world evidence. PMPRB officials agreed that a transparent evaluation plan should be put in place and reported on annually.

The final report was published on July 5, 2019.

The PMPRB will publish draft Guidelines for public consultation once the Board has had an opportunity to review the Steering Committee's report and following final publication of the amended *Patented*

*Medicines Regulations* in Part II of the Canada Gazette. Details on the nature and scope of the public consultation will be made available at that time.

The PMPRB would like to thank members of the Steering Committee for their participation in this phase of the consultative process and looks forward to an open and constructive consultation process on its new Guidelines in the coming months.

## 8. Written submissions

8.1. July 13, 2018 IMC questions to PMPRB re Working Group

8.2. July 15, 2018 letter from CORD to PMPRB

8.3. July 19, 2018 letter from PMPRB to CORD

8.4. September 6, 2018 CORD Feedback to August 15, 2018 meeting

8.5. September 6, 2018, MOHLTC Feedback to August 15, 2018 meeting

8.6. September 7, 2018 Myeloma Canada Feedback to August 15, 2018 meeting

8.7. September 7, 2018, BIOTECanada Feedback to August 15, 2018 meeting. Resent in response to Steering Committee Questionnaire, April 8, 2019

8.8. December 13, 2018, BIOTECanada Case Studies

8.9. March 29, 2019, BIOTECanada and IMC Questions and Comments to Steering Committee Regarding the Technical Working Group Report.

8.10. April 5, 2019, Gastrointestinal Society/Best Medicines Coalition response to Steering Committee Questionnaire

8.11. April 7, 2019, Owen Adams response to Steering Committee Questionnaire

8.12. April 8, 2019, IMC response to Steering Committee Questionnaire

8.13. April 8, 2019, CORD and Myeloma Canada Open Letter to the Prime Minister in response to Steering Committee Questionnaire

8.14. May 22, 2019, Dr. Paulden letter to Prime Minister - Clarifications of the Mandate and Recommendations of the PMPRB 'Working Group'

8.15. April 16, 2019, Canadian Life and Health Insurance Association response to Steering Committee Questionnaire

8.16. May 3, 2019 Mitch Moneo response to Steering Committee Questionnaire

8.17. May 13, 2019, BIOTECanada email and final case studies

8.18. May 17, 2019, IMC email to Steering Committee

8.19. May 27, 2019, BIOTECanada letter to Dr. Levine, PMPRB modernization initiative's Steering Committee process

8.20. May 27, 2019, IMC Correspondence to Dr. Mitchell Levine

8.21. June 27, 2019, Dr. Levine Correspondence to IMC

# 9. Appendix

## 9.1. Terms of Reference

### 9.1.1. Patented Medicine Prices Review Board (PMPRB) Terms of Reference for Steering Committee on Modernization of Price Review Process Guidelines

### 9.1.2. Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines Terms of Reference

## 9.2. Materials Presented at Meetings and Background

### 9.2.1. PMPRB Framework Modernization: Presentation to Steering Committee June 25, 2018

### 9.2.2. Assessing health opportunity costs for the Canadian health care systems. Ochalek J., Lomas J. and Claxton K. University of York. March 12, 2018

### 9.2.3. Canada Gazette – Regulations Amending the Patented Medicines Regulations, Regulatory Impact Analysis Statement, December 2, 2017

### 9.2.4. IHE White paper: Theoretical models of the cost-effectiveness threshold, value assessment, and health care system sustainability. March 2018.

### 9.2.5. PMPRB Guidelines Scoping Paper: High Level Overview of Potential New Framework, December 2017

### 9.2.6. Guiding document for the second meeting of the Steering Committee on Modernization of Price Review Process Guidelines, August 15, 2018

### 9.2.7. Data Analysis to Inform Guidelines Modernization SC and TWG, August 27, 2018

### 9.2.8. Guiding document for the third meeting of the Steering Committee on Modernization of Price Review Process Guidelines, September 12, 2018

### 9.2.9. Guideline Modernization: Case Studies, December 13, 2018

### 9.2.10. Proposed Application of PE and Market Size Factors to Category 1 Drugs, December 13, 2018

### 9.2.11. Steering Committee Consultation Roadmap - Update, December 13, 2018

### 9.2.12. Final Report of the Working Group to Inform the PMPRB Steering Committee on Modernization of Price Review Process Guidelines, March 2019

### 9.2.13. Recommendations of the Technical Working Group, PowerPoint presentation, March 15, 2019

### 9.2.14. Steering Committee Questionnaire- March 20, 2019

### 9.2.15. PMPRB Steering Committee on Modernization of Price Review Process Guidelines PowerPoint presentation May 13, 2019

## 9.3. Steering Committee Meeting Minutes

### 9.3.1. Steering Committee Meeting June 25, 2018

### 9.3.2. Steering Committee Meeting July 24, 2018

| | |
|---|---|
| **From:** | Declan Hamill |
| **To:** | Matthew Kellison |
| **Cc:** | Douglas Clark; Guillaume Couillard; Linda Payant; Isabelle Demers; Pamela Fralick |
| **Subject:** | Request from PMPRB to Steering Committee re Questions for Working Group |
| **Date:** | Friday, July 13, 2018 3:30:10 PM |

Dear Matthew:

In its June 25, 2018 presentation to the Steering Committee, the PMPRB posed "technical questions for analysis and recommendation" for the proposed Working Group (Slide 25). The PMPRB requested that Steering Committee members identify further issues that they believe would benefit from expert review and analysis by July 13, 2018. As requested, IMC submits the questions set out below.

IMC understands that the PMPRB intends to take steps to modernize its Guidelines within the framework of the proposed amendments to the Regulations. While IMC is committed to constructive engagement with the PMPRB on Modernization of Price Review Process Guidelines, our participation on the Steering Committee and the Working Group should not be interpreted as supporting the proposed amendments to the Regulations. IMC continues to have serious policy and process concerns about the proposed amendments, and reserves its right to oppose the proposed amendments and the work of the Steering Committee and Working Group to the extent it is intended to implement or reflect the proposed amendments. IMC also has many concerns with the June 25, 2018 Guideline Proposals and will provide more detailed commentary once we have had an opportunity to fully assess their potential impacts on patentees.

For the time being and as requested, IMC submits the following questions, but would note that we may have additional questions as the process evolves.

- Based on the PMPRB's proposed screening criteria (Slide 15; 11) what proportion of products would be classified as Category 1 versus Category 2 (based on the last 2 years of new product launches)? Is the PMPRB's stated estimate of 20-30% in Category 1 as stated during the June 25, 2018 Steering Committee meeting accurate?
- How can manufacturers report private and public average prices when manufacturers do not sell directly to public and private payers?
- What is the rationale for the PMPRB to move from real ex-manufacturer pricing to a privately-owned data source that may not report comparable information and is not necessarily representative of the market?
- How can MRP be calculated when rebate invoices are not standardized (quarterly vs annually) and where significant time may elapse between market entry and invoice finalization? What if rebates are associated with only one indication of a medicine?
- At the time PMPRB is assessing ceiling price, manufacturers would in most cases not have any PLAs in place, and hence would have no rebated price to assess against an MRP. How can the proposals proceed in light of the numerous and fundamental feasibility issues?
- Economic evaluations of a drug are inherently subjective: different experts and HTA agencies can arrive at different QALY measures. How can the uncertainty of economic

evaluations possibly be managed in the quasi-judicial regulatory context?

- CADTH ICERs are only based on a public drug plan perspective and do not apply to the private payer market. What is the rationale for using this information when it mismatched to what is being regulated?
- How can a flat "Market size/GDP" threshold be applied to all Category 1 products when treatment and population dynamics differ significantly?
- Moving to an average TCC would be a major departure from established regulatory practice and reflects an unprecedented intervention in the market. What is the rationale for regulating on the basis of the number of products in the market, via the proposed average TCC? What will be the impact on market competition? How would an average TCC impact the number of competitors in the market in each current therapeutic class and future product launches in each therapeutic class?
- There are no market-based solutions in the June 25, 2018 slide deck. Did the PMPRB conducted any analysis that would support the apparent rejection of market-based solutions?
- The price test for Category 2 drugs is based on the list price (MLP), not a rebated price (MRP). What would happen for existing Category 2 drugs that already have a PLA in place?
- What would happen if a product with an MRP were to be de-listed?
- What would happen to products that receive a 'do not fund' recommendation from HTA bodies despite a positive Health Canada approval?
- Given the complexity of the June 25, 2018 Guidelines proposals and time it will take to understand and work through them, is it realistic for the Working Group to create a journal publication in the stated timeframe (November 2018)?

With Kind Regards,

Declan

**DECLAN HAMILL**

*Vice-President, Legal, Regulatory Affairs & Compliance | Vice-Président, Affaires juridiques et réglementaires, et Conformité*

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Canadian Organization for Rare Disorders

15 July 2018

Douglas Clark
Executive Director
Patented Medicine Prices Review Board / Government of Canada

Dear Doug,

You invited feedback and suggestions for further work following the Steering Committee meeting June 25.

First, thank you very much for setting up the Steering Committee and for a highly engaging first meeting. I found that, for the most part, there was time and an atmosphere conducive to open and honest exchange. There were many perspectives raised and discussed. I realize I am not clear as to the intended format for capturing the discussion or producing a record of key points. I don't believe we were asked to arrive at any consensus at this time nor were we were actually asked to provide specific recommendations as a Steering Committee. I would appreciate clarification of how we will work to provide guidance as a Steering Committee and how discussions in person, by teleconference, or perhaps even by electronic media, will be captured and shared.

Second, I was in fact rather taken aback to learn at this first meeting that so many "key features of a new Guidelines framework" have already been determined. So, while one of our Committee mandates was to "operationalize amendments to the Patented Medicines Regulations," indeed the structure and the process of the Guidelines framework appear to be highly defined and the questions presented to the Steering Committee constituted minor refinements. The level of detail presented is all the more surprising based on your statement that there is not yet a final version of the Regulatory Amendments. For example, which aspects of the Proposed Price Review Schematic are embedded or are modifiable?

Third, there were many modifications to the proposed review process that appear to have changed since the first consultation, presumable reflecting the feedback that PMPRB has been receiving from various stakeholders. I felt I would have been able to contribute much more effectively if we had been presented with the information contained the slide deck in advance of the first meeting. As noted previously, we were not asked to arrive at consensus on recommendation, but frankly the time could have been used much more productively with pre-knowledge of the information and questions to be addressed.

Fourth, I fully appreciate the dilemma for the PMPRB in having to meet the Health Minister's deadline of February 2019 for an implementation plan while not having the final amendments. So while expediency appears to be the order, there is a tremendous risk to adopting the price review process presented. We know of no other jurisdiction that has applied pharmacoeconomics to set a universal "cost-per-QALY" threshold as the transparent maximum list price. Many jurisdictions, including Canada, do apply pharmacoeconomics as part of their health technology assessment and/or "value-based

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pricing" approach towards negotiating a reimbursement price, but many other factors are also considered in all articulated processes (factors such as alternative therapies, severity of disease, equity, and societal impact). In 2013, the UK proposed introduction of a "cost-per-QALY" threshold and asked NICE to develop evaluation methods. However, the feedback received from over 100 stakeholders during consultations was so overwhelmingly negative, the approach was formally abandoned in 2014 before any implementation.

Fifth, we have examined some of the OECD countries that have been cited as achieving lower drug costs to learn what they are doing. To the best of our knowledge, none are going down this path of a single "cost-per-QALY" threshold; indeed, most use pharmacoeconomics as only one of the factors in negotiating appropriate drug prices. Theoretically, this is the same approach currently used by Canada through CADTH, INESSS, pCPA, and the public drug programs. So, it begs the question: if comparable jurisdictions are using comparable HTA and negotiation processes, why would Canada be paying more for comparable patented medicines? What is Canada doing wrong?

Is the problem that Canada is starting with an inflated "list" price based on our current list of reference countries? If we were to change the basket of reference countries to eliminate higher priced countries (USA and Switzerland) and add countries at a lower price point, would this bring us more in line with the other OECD countries? It may be more helpful for us to consider the processes used by those countries that seemingly do a better job of managing prices and also achieving as good or better access to therapies for patients. We might suggest looking at Sweden, Germany, France, and Japan.

Given the fact that the final PMPRB regulatory amendments have not been submitted and the experience of a country like the UK that considered a similar approach, would Canadians not be better served if we were to have genuine consultations where all stakeholders could openly dialogue and consider the options for achieving our mutual goals of optimal drug expenditures, optimal access for patients, and continued support for innovation? The Steering Committee could serve to help "steer" the consultations and then engage in dialogue and deliberations on the options. This would allow us to provide genuine guidance to PMPRB and the governments on implementation of regulations that would meet our mutual goals.

Sixth, CORD has worked actively with payers and manufacturers to develop innovative approaches to reimbursement to help address the challenge of high cost drugs. For example, we encourage the use of managed entry programs that make coverage conditional on performance and we are prepared to work with payers on making these programs work based on evidence. If PMPRB guidelines deter a manufacturer from bringing a drug to market, patients will lose.

At the June 25 meeting, PMPRB presented a number of new proposals for the first time on other aspects of price guidelines. At the very least, if we are to continue down this path (preferably while also examining alternative pathways as proposed above), we request the following.

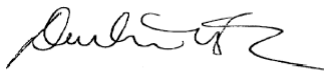
- PMPRB should provide several examples of how the proposed framework would apply in practice. At least one of these examples should be a rare disease drug.

- PMPRB should also explain how its new framework could impact the current HTA review by CADTH and price negotiation by pCPA. Will these processes be aligned? How will they impact timelines to final listing decision?
- PMPRB should identify the key elements of the new guidelines and schedule sufficient meetings of the steering committee to consult on them.

In light of the above, it is not feasible for the Steering Committee to engage in only three more meetings as planned and produce a report in the fall; the activities and timeline must be reassessed to ensure changes proposed will achieve desired benefits for all Canadians.

Thank you in advance for the opportunity to submit these thoughts and I look forward to your response.

Sincerely,



Durhane Wong-Rieger, PhD
President & CEO
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cc: Steering Committer Members
Minister of Health Ginette Petipas Taylor

Patented Medicine Prices Review Board Canada
Conseil d'examen du prix des médicaments brevetés Canada

Box L40, Standard Life Building
333 Laurier Avenue West, Suite 1400
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July 19, 2018

Ms. Durhane Wong-Rieger
President & CEO, Canadian Organization for Rare Disorders
151 Bloor Street West, Suite 600
Toronto, Ontario
M5S 1S4

Dear Ms. ~~Wong-Rieger~~ Durhane,

Thank you for your letter dated July 15, 2018, providing feedback on our recent Steering Committee meeting. It is encouraging to hear that you found the atmosphere at the meeting to be conducive to an honest and open exchange of views. This is a credit to our stakeholders and very much what we hoped for in gathering them all together in this manner. The positive overall tone of the meeting notwithstanding, you have raised a number of issues and concerns with respect to its subject matter and the process for addressing it going forward. For ease of reference, I will endeavor to respond to your points in the same order as they appear in your letter.

In terms of how Steering Committee members are to provide guidance and how it is to be captured and shared, PMPRB staff is serving as the secretariat to the Committee and taking meticulous notes of its deliberations. As explained in the Terms of Reference ("ToR") provided to Committee members prior to the first meeting, a report of the Committee's deliberations and any associated recommendations will be prepared by staff and provided to the Board for its consideration prior to publication of draft Guidelines for broader consultation. While we recognize that the nature of the underlying policy is such that consensus from our diverse stakeholder community cannot be expected, the Committee's co-chairs will make every effort to ensure that the final report accurately reflects any important points of convergence or contention between members.

I regret that you came away from the meeting with the impression that many key features of the PMPRB's new Guidelines have been predetermined. We made a concerted effort over the course of the meeting to give the opposite impression and I specifically stated in my opening remarks that nothing about the described approach has been set in stone.

We recognize and value the expertise and unique perspective of our stakeholders and the point of the Steering Committee exercise is to ensure that their views on key aspects of the regime are understood and addressed before developing draft Guidelines for broader public consultation. In order to achieve this goal, we were mindful that many of these same stakeholders, including industry and patient groups, have long held that greater detail about the proposed Guidelines is a necessary precondition to their providing meaningful feedback on reform to the PMPRB's regulatory framework. In providing the level of detail that we did, we were seeking to be responsive to that concern. I apologize if it gave rise to a more fatalistic interpretation by some in the room.

Lest any doubt remain on this question, let me assure you that nothing about the proposed Guidelines approach is embedded at this stage and virtually everything is modifiable. The consultation process is a fluid one, as evidenced by the modifications you reference in your letter, between the version of the Guidelines described in our December scoping paper and the approach presented to at the Steering Committee meeting. Your presumption that the modifications in question are the result of stakeholder feedback is an astute one, as they are borne of our desire to quell industry concerns about the potential indirect disclosure of confidential pricing information. That said, I take your point about the advantages of providing Steering Committee members with as much information as possible in advance of our meetings and we do try our best in that regard. However, we must balance this against our efforts to be as responsive as we can to stakeholder feedback on an ongoing basis given that we are operating under very tight timelines.

With respect to the proposed use of a cost-per-QALY threshold, we agree that a single universal threshold is not appropriate for all medicines and that pharmacoeconomics alone should not be determinative of price. That is why the model we are currently consulting on contemplates a variable threshold that accounts for the unique characteristics of certain high-cost drugs and their patient populations, and would apply a more generous threshold where it is appropriate to do so. Where these thresholds should ultimately be set, and the factors that should be taken into account when setting them, are precisely the kind of questions we are seeking feedback from the Steering Committee on, with the benefit of expert analysis from the Technical Working Group. As we explained at the meeting, assuming the regulations pass in their currently proposed form, pharmacoeconomic value is a factor that the PMPRB is legally obliged to operationalize. Our goal is to do so with a view to ensuring both the long-term sustainability of the Canadian healthcare system and Canadians continued access to the patented medicines they need to live healthy and productive lives.

To your point regarding pharmaceutical pricing policies in other OECD countries, our interaction with pricing and reimbursement authorities in most of these countries suggests to us that they are similarly struggling under the weight of a dramatic upsurge in high cost drugs. The different approaches to cost containment that we observe in these countries, including the manner in which they employ pharmacoeconomic analysis, arise from a need to tailor policy instruments to work within their own unique legal and health care systems. While Canada closely monitors regulatory developments in other countries to keep abreast of international best practices, perfect alignment with any one particular country model is neither practical nor desirable.

While it is true that list prices in Canada are higher than most other countries, this is not the only problem that the government is trying to address in advancing these reforms. As you know, in Canada and other developed countries, it has become common practice for pharmaceutical manufacturers to negotiate confidential rebates and discounts off public list prices in exchange for having their products reimbursed by public and private insurers. This empowers manufacturers to price-discriminate between buyers based on their countervailing power and perceived ability to pay. It also results in a growing discrepancy between public list prices and actual prices paid in the market. Accordingly, a key goal of the proposed reforms is to ensure that Canada's regulatory framework reflects the reality of today's marketplace. Under the approach described at the meeting, the PMPRB would continue to reference international list prices but apply a more probing and substantive analysis to high priority drugs to ensure that the prices Canadians truly pay for them are not unreasonable.

As for the nature and scope of the current consultation, while the proposed regulations are part and parcel of the of the government's comprehensive plan to improve the access, affordability and appropriate prescribing of prescription drugs in Canada, the PMPRB's policy remit is limited by section 96 of the *Patent Act* to issuing guidelines with respect to matters under its jurisdiction. While I can assure you that our efforts in this regard are genuine, we have no legal basis to engage with our stakeholders on the broader questions you raise in your letter.

With respect to your specific requests for the PMPRB to action, such as providing case studies for the new framework and explaining how the process the PMPRB envisages for administering its new Guidelines aligns with its partners, we agree that these are issues that should be considered by the Steering Committee as we go forward. On the latter point, the government's stated intention in advancing these reforms is to harness the strengths of various health partners, like the PMPRB, the pCPA, and CADTH, in a more integrated and collaborative approach to drug pricing in Canada. It is in no one's interest to duplicate our respective work or delay the market entry of new drugs to Canada.

Finally, while I recognize that there is a possibility that the January 2019 timeline may change, for the time being, our intention is to make our subsequent Steering Committee meetings as productive as possible in advance of further consultation on our draft Guidelines.

I trust that the above is responsive to your concerns and look forward to our next Steering Committee meeting on July 24.

Sincerely,

Douglas Clark
Executive Director

c.c. Honourable Ginette Petitpas Taylor, Minister of Health
Members of the PMPRB's Steering Committee on Guideline reform

| | |
|---|---|
| **From:** | Durhane Wong-Rieger |
| **To:** | Claudia Lacroix |
| **Cc:** | Suzanne (MOHLTC) McGurn; Imran (MOHLTC) Ali; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; Brian O'Rourke; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; Stephen Frank; Jim Keon; jody@canadiangenerics.ca; Christina@canadiangenerics.ca; Laurene Redding; Paul.Petrelli@jazzpharma.com; Pamela Fralick; dhamill@imc-mnc.ca; jeff.blackmer@cma.ca; owen.adams@cma.ca; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; Gail Attara; Martine Elias; Doidge, Scott: HC; Susan Pierce; Brittany Nagy; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; lynnm@cadth.ca; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; chantale.beauchamp2@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; gfreund@imc-mnc.ca; pclement@imc-mnc.ca; Karen.Clark@cma.ca; ryan.redecopp@canada.ca; megan.steen@canada.ca; Linda Payant; Guillaume Couillard; Tanya Potashnik; Matthew Kellison |
| **Subject:** | Re: Seeking feedback on questions presented during the August 15th Steering Committee on Guideline reform meeting |
| **Date:** | Thursday, September 6, 2018 5:31:56 PM |

Sorry, this got away before I finished the thought.

T1. I really don't feel we have been given enough information by way of research, evidence, sensitive testing, and case tests to make a cogent response. Given the considerable time to get to market through the public drug plans, it is equally likely that we will not have a negotiated price within 3 years or that both sides will delay to achieve greater certainty, which would be a problem for patients. Moreover how does Canada include in value calculation industry-provided resources such as patient support programs, which are not included in other jurisdictions like the UK.

T3. Given our complete objection to the use of HTA/ICER or other value propositions to set Maximum List Price, there is no answer that we can give to this question. We feel these are wasted resources when applied by the PMRPB at this stage and definitely for many of these drugs that are first in class, without comparable therapies to determine "incremental value" and without sufficient evidence to determine the $/QALY with confidence. We need to explore more reasonable, useful, and appropriate approaches, especially for those rare, precision, or other therapies without easy comparison.

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> On Sep 6, 2018, at 5:05 PM, Durhane Wong-Rieger <durhane@sympatico.ca> wrote:
>
> It is nigh near impossible to provide an informed (evidence) based response to

these questions without considerable more information and discussion. In terms of question 1, on what basis has PMPRB proposed 7 countries and 3 years? While we note the supporting document that, it is not clear that prices don't change (much) after 3 years and "x-amount" oft sales or time. Moreover, the comparison across any one point in time misses potentially significant differences on many relevant dimensions, induing resources provided by the system (or not) as well as other contributions obliged by the payer to the provider to achieve listing.

We do not agree with fixing the countries as "set in stone" whereas the comparison indices as set in stone.

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On Aug 27, 2018, at 3:25 PM, Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca> wrote:

Dear Members,

Following our last meeting on August 15th, I am writing to seek your written feedback on the questions presented during the meeting by no later than September 6th, 2018. This will allow us to prepare for the next meeting which is tentatively planned for September 12th (confirmation and details to follow later this week). In order to facilitate this, a presentation which includes high level data analysis has been made available on Brite Share.

Thank you in advance for your feedback.

Tanya Potashnik et Matthew Kellison
Co-Chairs

**Objet: Recherche de commentaires sur les questions présentées lors de la réunion du Comité directeur du 15 août sur la réforme des lignes directrices**

Chers membres,

Suite à notre dernière réunion, le 15 août, je vous écris pour obtenir vos commentaires écrits sur les questions présentées lors de la réunion au plus tard le 6 septembre 2018. Cela nous permettra de préparer la prochaine réunion qui est provisoirement prévue pour le 12 septembre ( confirmation et détails à suivre plus tard cette semaine). Pour faciliter cela, une présentation incluant une analyse de données de haut niveau a été mise à disposition sur Brite Share.

Merci d'avance pour vos commentaires.

Tanya Potashnik et Matthew Kellison
Co-Présidents

*Claudia Lacroix*

Executive Assistant to the Director
Board Secretariat, Communications and Strategic Planning
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<PMPRB_data_analysis_SC_TWG_GUIDELINES_final.pdf>

-------- Original message --------
From: "McGurn, Suzanne (MOHLTC)" <Suzanne.Mcgurn@ontario.ca>
Date: 2018-09-06 11:46 AM (GMT-05:00)
To: Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca>, Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
Cc: "Ali, Imran (MOHLTC)" <Imran.S.Ali@ontario.ca>
Subject: RE: Seeking feedback on questions presented during the August 15th Steering Committee on Guideline reform meeting

Good afternoon

Thank you for the reminder and the opportunity to respond.

Question1: Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?
Response: Yes, based on the information presented, it seems like a feasible approach. I suspect payors will prefer in general even greater certainty, but I am hoping that if implanted as proposed, that it will be monitored to see what the variability in pricing is over the 3 year time period to determine whether further adjustments are required.

Question 2: Is the proposed division and treatment of Category 1 and Category 2 drugs a reasonable risk-based regulatory approach?
Response: I don't profess to fully well versed in the breadth of risk-based regulatory approaches but I would say the proposed approach seems reasonable. A few general comments.

- Bullet #1 First in class or substantial improvement over existing drugs for clinically significant indications.
  - I have highlighted the words that I think we need to develop some common understanding of, if this is to be an effective filter
- Market Size > Affordability Threshold
  - Think we need to be clear if this means by 'indication' or stacked indications
- ICER
  - Ok

- Annual treatment cost > per capita GDP
  - Ok

Hope this is helpful

*Suzanne*



---

**From:** Claudia Lacroix [mailto:claudia.lacroix@pmprb-cepmb.gc.ca]
**Sent:** August-27-18 3:26 PM
**To:** McGurn, Suzanne (MOHLTC); Ali, Imran (MOHLTC); michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; sfrank@clhia.ca; jim@canadiangenerics.ca; jody@canadiangenerics.ca; Christina@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; pfralick@imc-mnc.ca; dhamill@imc-mnc.ca; durhane@optimizinghealth.org; durhane@sympatico.ca; jeff.blackmer@cma.ca; owen.adams@cma.ca; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; gail@badgut.org; melias@myeloma.ca; Doidge, Scott: HC; susan.pierce@canada.ca
**Cc:** Nagy, Brittany (MOHLTC); Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; lynnm@cadth.ca; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; chantale.beauchamp2@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; gfreund@imc-mnc.ca; pclement@imc-mnc.ca; Karen.Clark@cma.ca; ryan.redecopp@canada.ca; megan.steen@canada.ca; Linda Payant; Guillaume Couillard; Tanya Potashnik; Matthew Kellison; Claudia Lacroix
**Subject:** Seeking feedback on questions presented during the August 15th Steering Committee on Guideline reform meeting

Dear Members,

Following our last meeting on August 15th, I am writing to seek your written feedback on the questions presented during the meeting by no later than September 6th, 2018. This will allow us to prepare for the next meeting which is tentatively planned for September 12th (confirmation and details to follow later this week). In order to facilitate this, a presentation which includes high level data analysis has been made available on Brite Share.

Thank you in advance for your feedback.

Tanya Potashnik et Matthew Kellison
Co-Chairs

**Objet: Recherche de commentaires sur les questions présentées lors de la réunion du Comité directeur du 15 août sur la réforme des lignes directrices**

Chers membres,

Suite à notre dernière réunion, le 15 août, je vous écris pour obtenir vos commentaires écrits sur les questions présentées lors de la réunion au plus tard le 6 septembre 2018. Cela nous permettra de

préparer la prochaine réunion qui est provisoirement prévue pour le 12 septembre ( confirmation et détails à suivre plus tard cette semaine). Pour faciliter cela, une présentation incluant une analyse de données de haut niveau a été mise à disposition sur Brite Share.

Merci d'avance pour vos commentaires.

Tanya Potashnik et Matthew Kellison
Co-Présidents

*Claudia Lacroix*

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secrétariat du Conseil, communications et planification stratégique
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| | |
|---|---|
| **From:** | Martine Elias |
| **To:** | Durhane Wong-Rieger; Claudia Lacroix |
| **Cc:** | Suzanne (MOHLTC) McGurn; Imran (MOHLTC) Ali; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; Brian O'Rourke; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; Stephen Frank; Jim Keon; jody@canadiangenerics.ca; Christina@canadiangenerics.ca; Laurene Redding; Paul.Petrelli@jazzpharma.com; Pamela Fralick; dhamill@imc-mnc.ca; jeff.blackmer@cma.ca; owen.adams@cma.ca; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; Gail Attara; Doidge, Scott: HC; Susan Pierce; Brittany Nagy; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; lynnm@cadth.ca; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; chantale.beauchamp2@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; gfreund@imc-mnc.ca; pclement@imc-mnc.ca; Karen.Clark@cma.ca; ryan.redecopp@canada.ca; megan.steen@canada.ca; Linda Payant; Guillaume Couillard; Tanya Potashnik; Matthew Kellison |
| **Subject:** | Re: Seeking feedback on questions presented during the August 15th Steering Committee on Guideline reform meeting |
| **Date:** | Friday, September 7, 2018 12:59:07 PM |
| **Attachments:** | image001.png |

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Hi all,
Thank you Durhane for representing the patient perspectives on these questions.

I would also like to emphasise the point on the lack of background information that is necessary to better understand the recommendations made here, which I am assuming are made by the technical committee. For us (patient representatives) to make cogent responses it would be good to have the technical committee walk us through their data and assumption using case scenarios, where we can better understand the risks that patients can be exposed to.

More specifically for T3:
Walking us through an example for examples using the suggested :

- 75% of pCODR drugs fell between $100k-$300k/QALY
- 55% of CDR drugs were below $100k/QALY

Would be useful as it would seem that most drugs falling into these categories would have significant pressure to price reductions. It would also allow us to better undertand the thinking behind these suggestions.

I am in total agreement with Durhane's comment regarding exploring other options especially for rare, high impact outcomes, and would suggest that a different set of parameters by explored and I would like to see interested stakeholders come to the table with some suggestions, because this is where patients are and will be the most impacted.

Have a great weekend all,

**Martine Elias** MSc
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**From:** Durhane Wong Rieger <durhane@sympatico.ca>
**Date:** Thursday, September 6, 2018 at 5:31 PM
**To:** Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca>
**Cc:** "Suzanne (MOHLTC) McGurn" <Suzanne.Mcgurn@ontario.ca>, "Imran (MOHLTC) Ali" <Imran.S.Ali@ontario.ca>, "michael.sherar@cancercare.on.ca" <michael.sherar@cancercare.on.ca>, "robin.mcleod@cancercare.on.ca" <robin.mcleod@cancercare.on.ca>, Brian O'Rourke <BrianO@cadth.ca>, "luc.boileau@inesss.qc.ca" <luc.boileau@inesss.qc.ca>, "sylvie.bouchard@inesss.qc.ca" <sylvie.bouchard@inesss.qc.ca>, "Karen.reynolds@canada.ca" <Karen.reynolds@canada.ca>, "eric.dagenais@canada.ca" <eric.dagenais@canada.ca>, "rodrigo.arancibia@canada.ca" <rodrigo.arancibia@canada.ca>, Stephen Frank <sfrank@clhia.ca>, Jim Keon <jim@canadiangenerics.ca>, "jody@canadiangenerics.ca" <jody@canadiangenerics.ca>, "Christina@canadiangenerics.ca" <Christina@canadiangenerics.ca>, Laurene Redding <laurene.redding@astrazeneca.com>, "Paul.Petrelli@jazzpharma.com" <Paul.Petrelli@jazzpharma.com>, Pamela Fralick <pfralick@imc-mnc.ca>, "dhamill@imc-mnc.ca" <dhamill@imc-mnc.ca>, "jeff.blackmer@cma.ca" <jeff.blackmer@cma.ca>, "owen.adams@cma.ca" <owen.adams@cma.ca>, "gdoucet@pharmacists.ca" <gdoucet@pharmacists.ca>, "jwalker@pharmacists.ca" <jwalker@pharmacists.ca>, Gail Attara <gail@badgut.org>, Martine Elias <melias@myeloma.ca>, "Doidge, Scott: HC" <scott.doidge@hc-sc.gc.ca>, Susan Pierce <susan.pierce@canada.ca>, Brittany Nagy <Brittany.Nagy@ontario.ca>, "Charlotte.elagab@gov.bc.ca" <Charlotte.elagab@gov.bc.ca>, "Rajni.Vaidyaraj@cancercare.on.ca" <Rajni.Vaidyaraj@cancercare.on.ca>, "adriana.ruiz@cancercare.on.ca" <adriana.ruiz@cancercare.on.ca>, "lynnm@cadth.ca" <lynnm@cadth.ca>, "annie.gariepy@inesss.qc.ca" <annie.gariepy@inesss.qc.ca>, "celine.makischuk@canada.ca" <celine.makischuk@canada.ca>, "chantale.beauchamp2@canada.ca" <chantale.beauchamp2@canada.ca>, "amanda.janes@canada.ca" <amanda.janes@canada.ca>, "adsa@clhia.ca" <adsa@clhia.ca>, "gfreund@imc-mnc.ca" <gfreund@imc-mnc.ca>, "pclement@imc-mnc.ca" <pclement@imc-mnc.ca>, "Karen.Clark@cma.ca" <Karen.Clark@cma.ca>, "ryan.redecopp@canada.ca" <ryan.redecopp@canada.ca>, "megan.steen@canada.ca" <megan.steen@canada.ca>, Linda Payant <linda.payant@pmprb-cepmb.gc.ca>, Guillaume Couillard <guillaume.couillard@pmprb-cepmb.gc.ca>, Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>, Matthew Kellison <matthew.kellison@pmprb-cepmb.gc.ca>
**Subject:** Re: Seeking feedback on questions presented during the August 15th Steering

Committee on Guideline reform meeting

Sorry, this got away before I finished the thought.

T1. I really don't feel we have been given enough information by way of research, evidence, sensitive testing, and case tests to make a cogent response. Given the considerable time to get to market through the public drug plans, it is equally likely that we will not have a negotiated price within 3 years or that both sides will delay to achieve greater certainty, which would be a problem for patients. Moreover how does Canada include in value calculation industry-provided resources such as patient support programs, which are not included in other jurisdictions like the UK.

T3. Given our complete objection to the use of HTA/ICER or other value propositions to set Maximum List Price, there is no answer that we can give to this question. We feel these are wasted resources when applied by the PMRPB at this stage and definitely for many of these drugs that are first in class, without comparable therapies to determine "incremental value" and without sufficient evidence to determine the $/QALY with confidence. We need to explore more reasonable, useful, and appropriate approaches, especially for those rare, precision, or other therapies without easy comparison.

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> On Sep 6, 2018, at 5:05 PM, Durhane Wong-Rieger <durhane@sympatico.ca> wrote:
>
> It is nigh near impossible to provide an informed (evidence) based response to these questions without considerable more information and discussion. In terms of question 1, on what basis has PMPRB proposed 7 countries and 3 years? While we note the supporting document that, it is not clear that prices don't change (much) after 3 years and "x-amount" oft sales or time. Moreover, the comparison across any one point in time misses potentially significant differences on many relevant dimensions, induing resources provided by the system (or not) as well as other contributions obliged by the payer to the provider to achieve listing.
>
> We do not agree with fixing the countries as "set in stone" whereas the comparison

indices as set in stone.

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On Aug 27, 2018, at 3:25 PM, Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca> wrote:

Dear Members,

Following our last meeting on August 15th, I am writing to seek your written feedback on the questions presented during the meeting by no later than September 6th, 2018. This will allow us to prepare for the next meeting which is tentatively planned for September 12th (confirmation and details to follow later this week). In order to facilitate this, a presentation which includes high level data analysis has been made available on Brite Share.

Thank you in advance for your feedback.

Tanya Potashnik et Matthew Kellison
Co-Chairs

**Objet: Recherche de commentaires sur les questions présentées lors de la réunion du Comité directeur du 15 août sur la réforme des lignes directrices**

Chers membres,

Suite à notre dernière réunion, le 15 août, je vous écris pour obtenir vos commentaires écrits sur les questions présentées lors de la réunion au plus tard le 6 septembre 2018. Cela nous permettra de préparer la prochaine réunion qui est provisoirement prévue pour le 12 septembre ( confirmation et détails à suivre plus tard cette semaine). Pour faciliter

cela, une présentation incluant une analyse de données de haut niveau a été mise à disposition sur Brite Share.

Merci d'avance pour vos commentaires.

Tanya Potashnik et Matthew Kellison
Co-Présidents

*Claudia Lacroix*

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<PMPRB_data_analysis_SC_TWG_GUIDELINES_final.pdf>

# BIOTECanada Response to the August 15, 2018 PMPRB Steering Committee Questions

BIOTECanada is committed to contributing constructively to the Steering Committee process. Responses to these questions does not predicate BIOTECanada's acceptance of the various aspects, but in the spirit of responding, please find the answers below.

**Use of External Price Referencing Question for Consideration**

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

    - It is not evident that the PMPRB12 is the appropriate basket and more appropriate baskets should be under consideration. The US should be included since the US is Canada's largest trading partner and its market structure is most similar to Canada; more work is required to identify the appropriate "price" to use for the US. Moreover, the complexity of reporting prices from twelve markets is exacerbated by the variation and inconsistency in market dynamics, availability of price sources, availability of dosage forms regimens, and approved indications among the countries.
    - Furthermore, the PMPRB's stated intention to use IQVIA MIDAS data for verification purposes is improper. The IQVIA MIDAS data are not publicly available ex-factory prices as required by the Regulations but rather an average calculation of sales against units that can vary year over year despite no actual price changes. IQVIA MIDAS prices are also highly variable, inaccurate and possibly unavailable when it comes to rare disease drugs due to the very small numbers of patients and the assumed markups. Additionally, it is evident from the PMPRB Annual Reports the IQVIA MIDAS international "prices" differ significantly and are usually lower than the PMPRB verified ex-factory prices reported by patentees under the current Regulations.

    **<u>Existing Patented Medicines:</u>**

    - Applying the MIPC in addition to changing the basket of reference countries to existing medicines is unfair and inappropriate given that existing medicines entered the market in good faith and in compliance with PMPRB policies and market conditions in place at the time. The

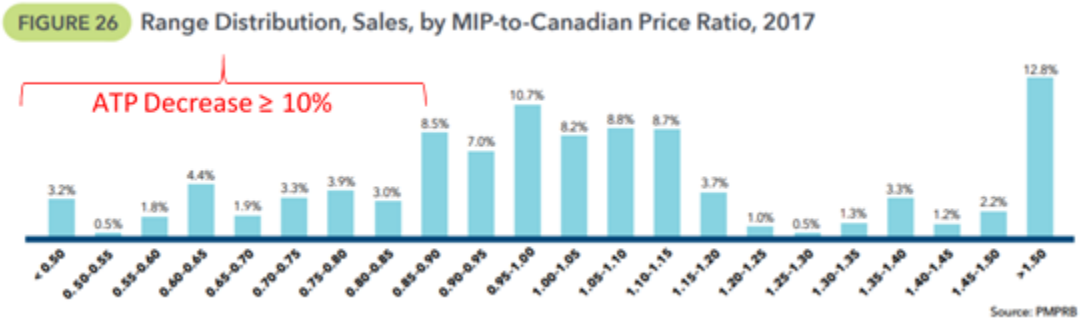
proposed changes are so significant that for many products it would bring into question their ongoing commercial viability.

- It is estimated that limiting the MLP to the median international price would impact more than 2/3 of products and would require a price reduction of approximately 29% on average for these products.[1] Such a significant, sudden reduction would have a dramatic negative impact on the Canadian pharmaceutical sector and, combined with the proposals for new patented medicines below, would threaten the availability of certain medicines for Canadian patients.
- The impact on ATP is uncertain. The PMPRB and the Minister in recent communications have both claimed that Canadian prices are on average 25% above the OECD median. Canadian average transaction prices would therefore need to decrease by 20% on average to reach the OECD median for which the proposed PMPRB12 is a proxy. As some patented medicines are already below the PMPRB12 median, the impact of those above will be even greater than the 20% average for all patented medicines.
- In a recent presentation (CORD webinar[2]), the PMPRB has asserted that "the proposed reforms are expected to have only a modest impact on prices, gradually reducing average prices of patented drugs in Canada by about 11% over the next 10 years". This statement does not align with the PMPRB's own analysis of the impact of the PMPRB12 / OECD median quite apart from the impact of the health economic and market size factors.
- **NOTE**: If a "gradual 11% reduction over the next 10 years" is an acceptable outcome to the PMPRB, there are more efficient mechanisms for achieving this outcome than the proposed risk- based approach. For example, an updated and appropriate basket of reference countries (less impactful than the PMPRB 12) combined with minor tweaks to the current guidelines would likely achieve this result. And without all the uncertainty associated with current complex proposals.
- The current proposals are intended to apply to all medicines as of January 2019. The reference to "gradual" necessarily assumes

[1] PDCI Market Access Analysis of 110 top selling patented medicines
[2] Canadian Organization for Rare Diseases (CORD), August 29, 2018, Presentation by Tanya Potashnik, PMPRB

transitional / grandfathering provisions that have yet to be disclosed or discussed.

- Figure 26 from the PMPRB 2017 Annual Report indicates that approximately 50% drug products have average transaction prices in excess of the PMPRB7 median. And approximately 1/3 of products would face a price reduction of greater than 10% (see Figure 26 from PMPRB 2017 Annual Report). Presumably the proposed PMPRB12 median would result in even greater proportions of patented medicines facing significant decreases in average transaction price.




- It must be noted that the differential between list price and ATP is not only discounts or rebates but, in many cases, "other benefits" such as the substantive cost of providing patient support programs, co-pay assistance, infusion clinics and services, compassionate drug programs, etc. Many of these programs have been developed and implemented by manufacturers to facilitate reasonable, efficient access to medicines, filling gaps in the structures of the provincial healthcare systems that benefit payers, healthcare providers, patients and caregivers. This is particularly true for high cost drugs and drugs for rare diseases. Lowering the MLP will threaten the viability of these programs delaying patient access to these drugs and/or potentially shifting some costs (e.g., infusion clinics, nurse support) from the manufacturer to patients. In other jurisdictions, these injection and support service costs are borne by the health care system and not the manufacturer.

New Patented Medicines:

- It is BIOTECanada's position that the PMPRB12 is NOT the appropriate basket of reference countries. For new medicines, the MIPC test could be appropriate but only in the context of the current Guidelines and if the there is an appropriate basket of countries.
- The current proposals make no reference to the level of innovation as a factor in assessing drug prices. Canada was one of the first countries to categorize new patented medicines by level of therapeutic improvement. This approach is common in many of the proposed reference countries including France, Germany, Italy and Japan and should continue to be the case in Canada.

2. **Should exceptions be made to the MLP-MIPC test and, if so, when and why?**
   - The MIPC test should only apply to new medicines and should not be the limiting factor – for example products with a TCC greater than MIPC but lower than HIPC should continue to be considered to be within Guidelines.
   - Existing medicines should be exempt and their current prices grandfathered as long as they remain within HIPC.
3. **Should there be a price floor for Category 2 medicines based on LIPC?**
   - LIPC floor should apply to all medicines not just category 2 medicines. No product price should be forced below the LIPC and any product with a price below LIPC can increase to the LIPC without any PMRPB limitations.
   - Moreover, the ATCC test is not appropriate. By definition, a medicine should not be considered "excessive" if older, therapeutically equivalent products have higher prices that are considered to be non-excessive. Furthermore, the ATCC test is a barrier to entry for new patented medicines particularly for innovative products entering older established therapeutic classes. For some drugs, the ATCC test will cause manufacturers to either not bring the product to Canada or withdraw the product from the Canadian market.
   - Line extension medicines should continue to be review with reference to the reasonable relationship test and the HIPC.

4. **Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?**

    - It is BIOTECanada's position that the PMPRB12 is not the appropriate basket of reference countries. Any basket of reference countries should continue to include the US as the U.S. is arguably the most appropriate comparator to Canada[3].
    - There needs to be clarification on "annual review" – August 15 and 27th slides decks from PMPRB do not align. One deck suggests a re-bench every year whereas the other suggests a re-bench after 3 years, 7 countries whichever comes first (similar to the current Guidelines). Clarification on this point is required.
    - And if a product is re-benchmarked due to other factors, say a new indication, would this create yet another "interim" median price?
    - The current approach to resetting interim median price is reasonable (3 years or 5 countries, whichever comes first) – it is not clear why there would need to be a change. If the intention is to re-benchmark every year then this would be unreasonable – as a practical matter prices can only go down but never up.
    - Removing exchange effect is important – MIP should be frozen at introduction or in the case of an interim median, once the interim median has been re-benched and finalized.

5. **Should an increasing gap between MIPC and the MLP trigger a re-bench?**

    - No. Gaps between MIPC and MLP can be temporary and once prices are lowered it is very difficult or impossible to raise them again due to PMPRB guidelines and provincial pricing policies.

6. **Should EPR differ depending on category or vintage of the patented medicine?**

    - Existing patented medicines should be limited to the highest international price and new medicines should be held to the current guidelines tests (including the median where appropriate).

[3] BIOTECanada positions re: basket – Feb 2018 CG1 response

## Use of List and Net Price Ceilings

1. **Should a Category 1 medicine ever have more than one MRP?**

    - The concept of MRP as a price threshold is inappropriate. PMPRB's compliance activities should be limited to ensuring that the national average transaction price (N-ATP) does not exceed maximum list price (MLP). Moreover, "MRPs" anticipate the filing of confidential third-party rebates with PMPRB which BIOTECanada opposes. The requirement for patentees to report third party rebates appears to be inconsistent with PMPRB's mandate. The PMPRB's mandate is limited to ex-factory prices paid by customers who purchase directly from the patentee. Classes of customers that are based on final retail purchasers or third parties that reimburse drug costs are beyond the scope of the PMPRB's jurisdiction as outlined on the PMPRB's website: "The PMPRB regulates the "factory gate" prices and does not have jurisdiction over prices charged by wholesalers or pharmacies, or over pharmacists' professional fees."4 Third party rebates are calculated based on the marked-up final retail price and not the ex-factory price.
    - Moreover, as a practical matter these classes of customer are not a basis for reporting under the Regulations. When patentees sell to wholesalers or to pharmacies the patentee has no foreknowledge as to the class(es) of the final purchaser or payer (i.e., public, private, cash).
    - The use of separate MRPs for different indications is also problematic – for drugs with multiple indications the patentee has no foreknowledge as to the final use of each ex-factory sale. There is no mechanism by which manufacturers can report sales by indication.
    - The use of MRP will result in protracted investigations over several years with prices of patented medicines appearing to be excessive throughout. It will likely be at least two calendar years post introduction before PMPRB is able to begin analyzing the scope and extent of rebates provided by a patentee given that reconciliation and rebate payments by manufacturers can be retroactive up to 1 year after the sale of a product.

[4] http://www.pmprb-cepmb.gc.ca/about-us

2. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

    - The concept of MRP should be abandoned (see above)
    - There are reimbursement and confidential listing agreement considerations that go directly to addressing cost effectiveness and affordability. These elements will often be unavailable to the PMPRB and even with the reporting of confidential rebates (which BIOTECanada opposes and would be contrary to established legal precedent) the confidential rebates would not fully capture the terms of PLAs that address cost effectiveness and affordability.
    - Moreover, to the extent that market size is considered at all (which BIOTECanada opposes) the test should consider only the incremental cost impact to the health care system. This would be more consistent with the approach taken by provinces and other payers that are interested in the incremental budget impact. The PMPRB's concept of market size would penalize a product that offers budget saving by taking significant market share from more expensive products.
    - Overall the new Category 1 factors create pricing uncertainty and a significant risk that otherwise non-excessive introductory prices will be reduced arbitrarily to commercially unacceptable levels with follow-on impacts in other markets that reference Canadian prices either formally or informally. This uncertainty will in many cases result in delayed launches until the patentee has certainty regarding the impact the factors have on list and average transaction prices.

3. **Should confidential third-party pricing information only be used for compliance purposes?**

    - Confidential third-party information should not be used at all except if filed voluntarily by the patentee, for example in the context of a hearing. As a practical matter, the third-party pricing information contemplated in the draft Regulations is rarely available in a timely manner and certainly not within the 30 day from end of period time frame required in the Regulations.

## Re-Benching Criteria

1. **How often and in what circumstances should a medicine be re-benched?**

    - Manufacturers require certainty as to pricing rules - frequent re-benching creates pricing uncertainty. To the extent that re-benchmarking is appropriate it should be predictable and reasonable.
    - For drugs with multiple indications It is rarely possible for patentees to separate sales by indication or to establish indication specific list prices. The indication for which a patented medicine is used is determined by the prescribing physician and unknown to the patentee. Accordingly, re-benchmarking for new indications should not be implemented.

## Risk Assessment and Prioritization Criteria for Category 1 & 2 Medicines

1. **Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk based regulatory approach?**

    - No. The question pre-supposes that a "risk based" approach is appropriate. No other market relies on the risk-based approach proposed by the PMPRB. Furthermore, the PMPRB's methodology ignores the clinical effectiveness (level of improvement or additional benefit) a new drug offers. The level of improvement is the basis of categorization employed by France, Germany, Italy and Japan.

2. **Should further categories exist with difference treatment modalities?**

    - No – the "risk-based" approach is already flawed.

3. **Should more or less criteria be considered in screening a medicine as a higher risk and where should the line be drawn with respect to the criteria?**

    - Need to return to level of improvement for purposes of categorization, if categorization is necessary at all.

4. **Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds**

    - As has consistently been communicated as the BIOTECanada position, pharmacoeconomic, market size and GDP factors should not be used for either a screen or threshold tool.

- To the extent they are applied at all, market size and GDP factors should only apply solely as a screen.
- Pharmacoeconomic factors should not be used as either a screen or threshold. If the PMPRB feels it is obligated, as has been communicated, to what is in the draft regulations, to use pharmacoeconomics, it should solely be reserved for hearings in cases where cost effective prices appear to exceed PMPRB's international price thresholds.

5. **Should Category 2 medicines be scrutinized more or less than proposed?**

- Less. HIPC rule only

7 September 2018

| | |
|---|---|
| **From:** | Iman Mohamed |
| **To:** | briano@cadth.ca; jim@canadiangenerics.ca; Jody@canadiangenerics.ca; sfrank@clhia.ca; Jeff.Blackmer@cma.ca; gdoucet@pharmacists.ca; robin.mcleod@cancercare.on.ca; gail@badgut.org; mitch.moneo@gov.bc.ca; karen.reynolds@canada.ca; susan.pierce@canada.ca; eric.dagenais@canada.ca; Rodrigo.Arancibia@canada.ca; dhamill@imc-mnc.ca; pfralick@imc-mnc.ca; luc.boileau@inesss.qc.ca; melias@myeloma.ca; Imran.S.Ali@ontario.ca; Douglas Clark; Matthew Kellison; Tanya Potashnik; Suzanne.Mcgurn@ontario.ca; Jody@canadiangenerics.ca; durhane@optimizinghealth.org; jwalker@pharmacists.ca; scott.doidge@canada.ca |
| **Cc:** | laurene.redding@astrazeneca.com; paul.petrelli@jazzpharma.com |
| **Subject:** | BIOTECanada Feedback to Steering Committee |
| **Date:** | Monday, April 8, 2019 5:11:53 PM |
| **Attachments:** | 180907 BIOTECanada Response to the August 15 SC Questions FINAL.pdf |

Good afternoon,

On behalf of the BIOTECanada Steering Committee representatives, I am writing to respond to the PMPRB's request for feedback on the questions posed to Steering Committee members.

BIOTECanada submitted responses to the questions on September 7, 2018. Please refer to the original submission attached.

Best,
Iman

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BIOTECanada

# Impact of Proposed PMPRB Guidelines – Case Studies

Steering Committee Meeting

December 13, 2018
Ottawa, ON

# Summary

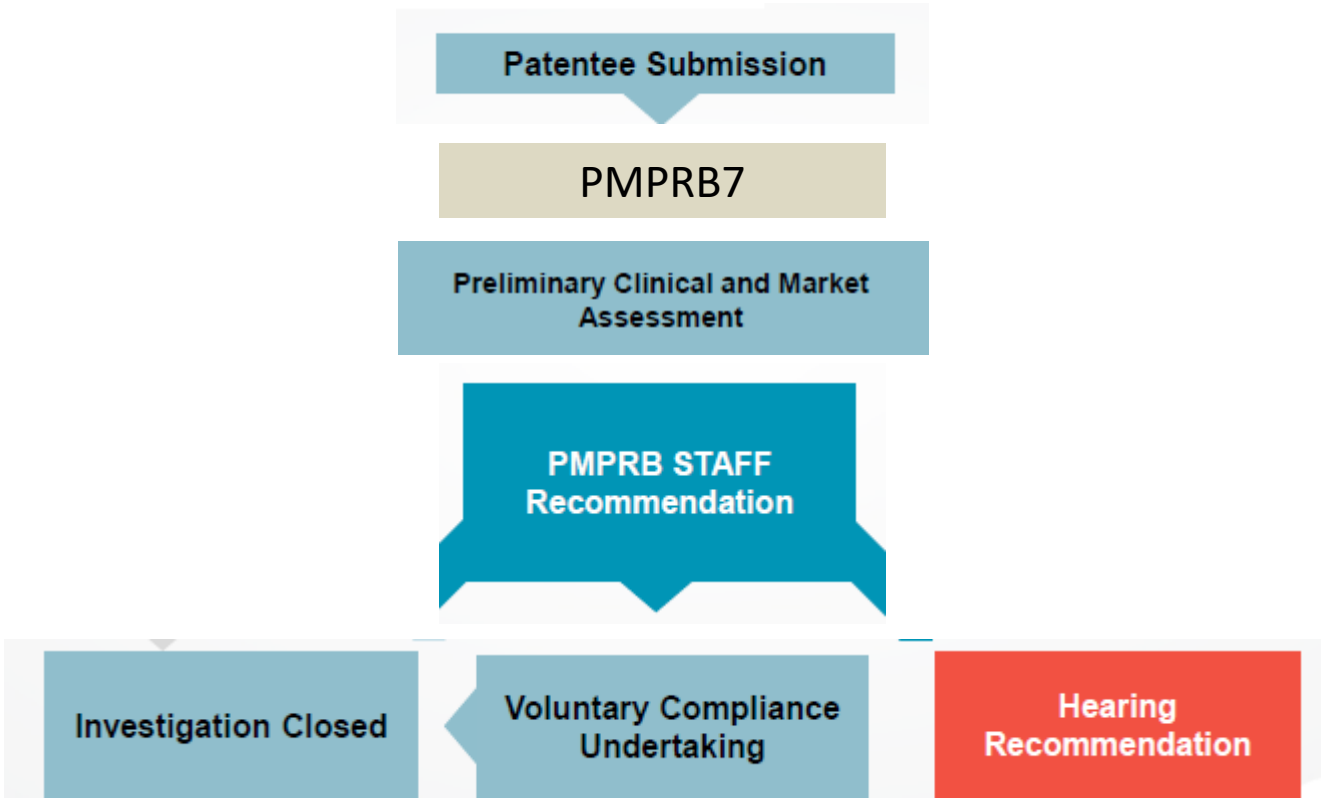
- Proposed guidelines create too much uncertainty
- Existing products, if launched under the proposed guideline, would not have been launched in Canada
  - Re-benching will create challenging decisions where manufacturers are in the position to have to decide whether to withdraw from the market
- The proposed guidelines do not create a “11% over 5 year” reduction, but instead create, for many products a significant reduction of more than 50% (not commercially viable).



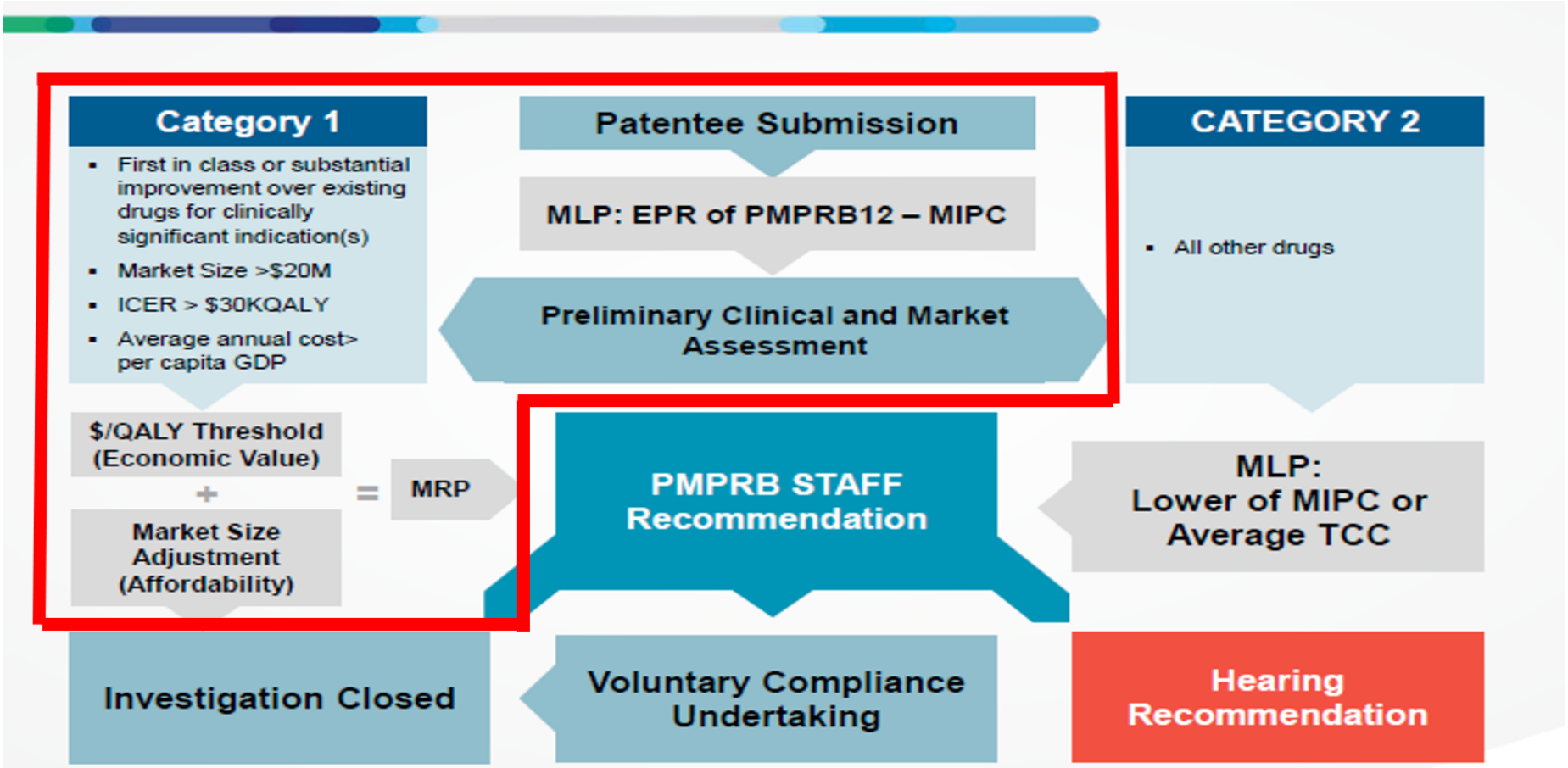
BIOTECanada

# Current Price Review Schematic

The current PMPRB system is a predictable evaluation that controls drug prices = regulatory & product launch certainty



# Changes proposed for Price Review



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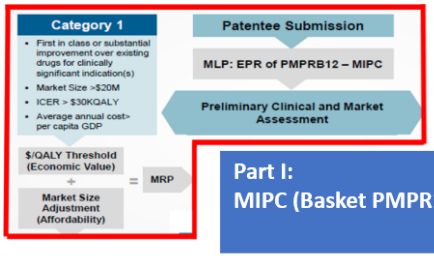
# PMPRB Proposal Assumptions




A complex series of evaluations leads to significant product launch uncertainty

| Part I: MIPC (Basket PMPR12) | Part II: Screening Criteria Category 1 or 2 | Part III: Step 1 Pharmacoeconomic Factors | Part III: Step 2 Market Size & GDP / GDP per capita | Part V**: Re-benching |
|---|---|---|---|---|
| MLP based on median of PMPRB12* (MIPC) | 1st in Class or substantial improvement over existing therapy | Category 1 > $60k/ QALY | MRP adjustment required if market size > $20M | All new drugs given interim MLP of 3yrs or until drug sold in 7 countries, whichever comes first |
| MIPC recalculated annually, or 3 yrs post first date of sale | Market Size > Affordability Threshold $20M per new drug w/in first 5yrs of sale | Higher $90-150k/QALY threshold "premium" new drug (high burden, DRD, significant absolute QALY gain) | $20M threshold will increase annually based on GDP growth and/or CPI | MLP and MRP frozen unless triggered |
| MLP adjusted over time (re-benching) | $60k/ QALY threshold for clinically significant indications | | 10% reduction on MRP for each additional $10M market size (to 50% max.) | Triggers:<br>- approval new indication<br>- Sales exceed market size<br>- New evidence of CE<br>- Significant change in int'l prices |
| IQVIA data to verify int'l prices | Avg. annual treatment costs above per capita GDP | | | Re-bench to increase price – with CE evidence, smaller market or significant increase in CPI |

* PMPRB12: Australia, Belgium, France, Germany, Italy, Japan, Netherlands, Norway, South Korea, Spain, Sweden, United Kingdom
** Part IV: applies only to category 2 drugs
MIPC = Median International Price Comparison
MLP = Maximum List Price
QALY = Quality Adjusted Life Year
GDP = Gross domestic Product
MRP = Maximum rebated price
CE = Cost effectiveness

# Overview of 3 Case Studies

Each of the therapies evaluated have been analyzed as per the current proposals outlined by PMPRB based on the information provided to date and have been:

- Approved by Health Canada
- Reviewed by CADTH
- Available in the Canadian marketplace

## Therapy 1:

- Small molecule capsule product for metastatic cancer
- 1400 patient population in Canada
- Moderate improvement (HDAP)
- No comparator

Too much variability in discount = product launch uncertainty

| Part I: MIPC (Basket PMPR12) | Part II: Screening Category 1 or Category 2 | Part III: Step 1 Pharmacoeconomic Factors | Part III: Step 2 Market Size & GDP / GDP per capita |
|---|---|---|---|
| MLP based on MIPC | Screened as Category 1 due to ICER threshold | Assuming $60k/ QALY threshold = 76% reduction required | Annual market size <$20M/year in first 5 years |
| | | Assuming $150k/QALY threshold = 0% reduction | |

Yellow = launch is highly unlikely

Red = launch will not happen



BIOTECanada

# Therapy 1: Oncology Therapy

Impact:

There is a wide variability in discount from cost effectiveness parameters.

If the proposed guidelines had been in place at the time of filing with Health Canada, launch in Canada unlikely or significantly delayed because price is too uncertain.

This therapy would continue to be available to patients in:

Argentina, Australia, Austria, Belgium, Bulgaria, Chile, Colombia, Denmark, Finland, France, Germany, Greece, Ireland, Israel, Italy, Lithuania, Luxembourg, Netherlands, Poland, Portugal, Russian Federation, Slovenia, Spain, Switzerland, Turkey, United States (NOT Canada).

## Therapy 2: Rare disease

- Addresses potential life threatening condition; most patients cannot work
- Less than 100 patients in Canada
- Significant clinical improvement granted a Health Canada Priority Review
-Moderate improvement(HDAP)
-No comparator

Additional discount barrier to launch created by PE factor

| Part I: MIPC (Basket PMPR12) | Part II: Screening Category 1 or Category 2 | Part III: Step 1 Pharmacoeconomic Factors | Part III: Step 2 Market Size & GDP / GDP per capita |
|---|---|---|---|
| MLP based on MIPC | Screened as Category 1 meets all the criteria slide 2 | Assuming $150k/ QALY threshold a 80% – 90% depending on the threshold | Annual market size greater than $20M/ yr. |
| | | | Range 10-50% additional reduction depending on how market size is applied |

Yellow = launch is highly unlikely

Red = launch will not happen



BIOTECanada

# Therapy 2: Rare Disease

Impact:

If proposed PMPRB guidelines had been in place at point of Health Canada filing, Canada would not be a globally competitive market based on maximum ceiling price demanding more than an 80% price reduction.

This therapy would continue to be available to patients in: Argentina, Austria, France , Germany, Greece, Italy, Norway, Portugal, Russia, Spain, Sweden, Czech, United States.

## Therapy 3: Autoimmune therapy, multiple indications

- new indications for adults with autoimmune disease
- Slight or no improvement (HDAP)
- Second new indication for different form of disease
- 85,000 to 100,000 patient population in Canada

PE factor + market size = price too low to make case for Canada

| Part I: MIPC (Basket PMPR12) | Part II: Screening Category 1 or Category 2 | Part III: Step 1 Pharmacoeconomic Factors | Part III: Step 2 Market Size & GDP / GDP per capita |
|---|---|---|---|
| MLP based on MIPC | Original indication: Category 1 due to ICER | Original indication: CDR required 30% reduction | Annual market size greater than $20M/ yr. An additional 50% reduction is required |
| | Second indication: Category 1 due to ICER | Second indication: CDR required 80% reduction | Range 0-50% additional reduction depending on how market size is applied |

Yellow = launch is highly unlikely

Red = launch will not happen



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# Therapy 3: Autoimmune treatment (multi indications)

Conclusion :

Canada does not get second important indication because price lowered 80% on first indication and 50% reduction on second indication, hence product may not launch in Canada for even first indication

The therapy would continue to be available to patients for first indication in:

Australia, Croatia, Denmark, Finland, Germany, Israel, Italy, Luxembourg, Netherlands, Switzerland, Turkey, United Arab Emirates, United States (NOT Canada)

The therapy would continue to be available to patients for new indication in:

Denmark, Finland, Germany, Israel, Italy, Latvia, Luxembourg, Netherlands, Switzerland, Turkey, United Arab Emirates, United States (Not Canada)



BIOTECanada

- Estimating the actual impact of the proposed regulations on prices depends critically on the way the regulations are operationalized through the Guidelines.
- Achieving closer integration among other agencies that are involved in the drug pricing process may be more important for achieving a system that properly balances objectives of patient and payer protection.

    - Dodge Report to Health Canada August 2018



BIOTECanada

**IMC/BIOTECanada Questions and Comments to Steering Committee Regarding the Technical Working Group Report**

On behalf of member companies of Innovative Medicines Canada (IMC) and BIOTECanada, we are writing to provide the industry's perspectives regarding the Steering Committee (SC) and Technical Working Group (TWG) processes.

The first SC meeting was held June 25, 2018 and the process over the ensuing nine-month period has brought to light significant deficiencies including the lack of clarity regarding the role, objectives and expected outcomes. Importantly, to date the SC forum has not allowed its members to provide true guidance to the PMPRB regarding two types of changes being contemplated by the PMPRB[1] namely:

> 1) the operationalization of the proposed amendments to the *Patented Medicines Regulations* (as opposed to input on the amendments themselves, which PMPRB also specifically excluded from the SC process); and
> 2) enabling the PMPRB to make more efficient the use of its resources by adopting a truly risk-based approach to how it regulates ceiling price that simplifies and streamlines compliance for patentees.

That these key elements have yet to be addressed since the SC's inception underscores the ongoing lack of meaningful consultation and input into proposed changes. Accordingly, if the proposed amendments are implemented without significant changes, it will lead to an uncertain business climate which could ultimately impact Canadian patients' access to innovative new medicines and therapies.

The concerns regarding the SC process were further highlighted by the March 15th, 2019 WebEx meeting where the Chair of TWG was invited to present the TWG's final recommendations to the SC. The months of work and deliberations of the TWG were minimized when the Chair of the TWG was placed in the challenging situation of having to present 143 slides summarize a technical 285-page report in a one-hour WebEx. This approach did not facilitate informing the process or SC members and did not allow any of the participants an opportunity to properly review or provide substantive input.

Notwithstanding the limitations set out above, regarding the TWG process, IMC and BIOTECanada would draw the SC's attention to industry and patient 'on-the-record' comments in Appendix 3 beginning on page 170. From this commentary it is apparent that, despite some agreement on high-

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[1] *PMPRB Terms of Reference for Steering Committee on Modernization of Prices Review Process Guidelines* http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1377&lang=en

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level recommendations, no consensus was reached at the TWG regarding the implementation of economic factors for the purpose of setting price ceilings for patented medicines in Canada.

In addition, there was no general agreement on cost effectiveness thresholds as an appropriate approach to consider opportunity cost and the TWG did not resolve the issue of how thresholds could be determined. Industry and other TWG members have identified issues related to uncertainty and lack of clarity, as well as the significant and, in many cases, insurmountable technical and operational issues associated with the application of these proposed economic factors.

1. Why has the PMPRB rejected any discussion of key 'feasibility' and implementation issues? This is particularly concerning as the TWG is the only forum specifically charged with consideration of technical questions related to implementation. In some cases, the feasibility issues that members attempted to raise are substantive enough that patentees subject to the proposed regulation changes do not currently have the ability to comply with the new reporting requirements.
2. Why are the recommendations frequently open ended and defer to the PMPRB's "policy intent"? In several cases, the TWG was unable to arrive at clear recommendations and ultimately determined that the questions posed could only be answered with further clarification of PMPRB's policy objectives.
3. Why has the PMPRB unilaterally imposed on the TWG the decision to adopt a public health care system perspective when the question of the appropriate perspective was assigned to the TWG for deliberation and recommendation?
4. Why were the case studies were only made available in the final stage of the TWG deliberations and a review and discussion of six individual case studies limited to only thirty-five minutes on the agenda of the one meeting where they were discussed?
5. Why is the magnitude of price reductions illustrated by these case studies depart so dramatically from what was determined by Health Canada's CG1 Regulatory Impact Analysis Statement and the Cost-Benefit Analysis?

We would also draw the SC's attention to the fact that "PMPRB clarified to the Working Group that its mandate is to protect consumers from excessive pricing, and not to ensure that products are launched into the market." This should give stakeholders some pause when considering the potential implications of proposed new economic factors on access to new medicines.

The decision of the PMPRB to disregard the TWG's deliberations of critical issues related to perspective, and the position that feasibility issues were out of scope for the TWG are particularly concerning and highlight the shortcomings of the TWG forum process.

Finally, and to reiterate our initial points above, we question what the SC's actual role is in relation to TWG report, and more broadly, what the the practical role of the SC is, given that it was not engaged in steering any tangible work streams at the TWG or elsewhere.

| | |
|---|---|
| **From:** | Gail Attara |
| **To:** | Tanya Potashnik; Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; sfrank@clhia.ca; jim@canadiangenerics.ca; jody@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; pfralick@imc-mnc.ca; dhamill@imc-mnc.ca; durhane@optimizinghealth.org; durhane@sympatico.ca; Blackmer, Jeff; Adams, Owen; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; melias@myeloma.ca; Doidge, Scott: HC; susan.pierce@canada.ca |
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| **Subject:** | RE: Next Steps for Steering Committee on Modernization of Price Review Process Guidelines |
| **Date:** | Friday, April 5, 2019 2:15:07 PM |
| **Attachments:** | 2018-02-14 BMC-PMPRB Regulations Submission.pdf<br>2018-12-05 BMC letter to PMPRB.pdf<br>2019-04-05 BMC response to PMPRB Questions.pdf |

Please see our attached letter (and attachments) in response to this request. We urge you to give full and careful consideration to all input from steering committee members, including those from other patient groups, whose positions we support.

Best regards,

Gail

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**Sent:** March 20, 2019 12:24 PM
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**Subject:** Next Steps for Steering Committee on Modernization of Price Review Process Guidelines

**Importance:** High

Dear Steering Committee Members,

In preparation for our last meeting please find attached a word document which contains all the questions that have been posed for the SC as part of the consultation process.

We introduced the proposed questions at our first face-to-face meeting June 25th , along with the proposed new PMPRB Guidelines Framework. Subsequent meetings focused on identifying possible topics for the Technical Working Group (TWG) as well as unpacking each aspect of the proposed framework and soliciting feedback. At our meeting in December, hypothetical case studies were presented in order to demonstrate how the framework could work in practice and provided an assessment of current guidelines relative to the proposed ones. Most recently, the SC received a copy of the Final Technical Working Group Report and the chair, Dr. M. Paulden, provided a webcast on the recommendations. We would like to offer the SC an additional opportunity to ask any follow up or clarifying questions on the TWG report. As has been the practice with feedback, please ensure to pose the questions with a cc to the entire SC before **March 29th**. Attached for your benefit is a copy of the presentation from the webcast.

We kindly ask you to provide your final formal feedback to the specific questions that had been identified by Board Staff on the attached questionnaire. Your responses along with other feedback that has already been received will be reflected in the final Steering Committee Draft report which we will circulate in advance of our next meeting. Steering Committee members will be provided with an opportunity to review the draft and ensure that we have accurately captured your feedback in the report. SC members will also be given an opportunity to speak to their feedback at the meeting to ensure everyone can hear the perspective directly.

We ask that you fill out the questionnaire by **April 8th.** We will be following up shortly with a doodle poll to see what dates work best for SC members in early May.

Sincerely,

**Tanya Potashnik**
Director, Policy and Economics Analysis Branch | Direction des politques et de l'analyse économique
Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés
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**Input Regarding Proposed Amendments to the Patented Medicines Regulations**

***Introduction:***

The Best Medicines Coalition (BMC) is a national alliance of 24 patient organizations with a shared goal of equitable and consistent access for all Canadians to safe and effective medicines that improve patient outcomes. Areas of interest include drug access, approval, assessment and reimbursement along with patient safety and supply concerns. The coalition strives to ensure that Canadian patients have a voice and are meaningful participants in policy development, specifically regarding pharmaceutical care.

As part of our efforts on behalf of Canadian patients, we welcome this opportunity to comment on the draft amendments to the Patented Medicines Regulations as published in Canada Gazette Part 1, December 2017 with a February 14 deadline for comments. This follows input the BMC submitted in June 2017 on Health Canada's proposed amendments, and in October 2016 regarding Health Canada's PMPRB Guidelines Modernization Discussion Paper.

***Pricing Regulation: Core Positions***

The BMC's input on the draft amendments to the Patented Medicines Regulations, as follows, is focused on those aspects directly related to patient interests and needs.

Please consider the following core positions:

- ***Balanced Oversight.*** The BMC supports a strong, balanced and fair regulatory framework for pharmaceutical pricing aimed at sustaining the life, health and wellbeing of patients. Such a framework should support early and sustainable access to innovations to meet unmet patient needs while also protecting patients and payers, and supporting current and ongoing effectiveness and sustainability of the health care system.

- ***Availability.*** A primary goal of pricing regulation, and indeed of all public bodies operating in the realm of pharmaceutical care, must be to contribute to an environment that facilitates the introduction and availability of a comprehensive range of medicines, including newly developed advancements to address unmet needs, and not hinder patient access to clinical trials.

- ***Timely Access.*** The ability to access necessary medicines in a timely manner is an important cornerstone of protecting and optimizing the health and wellbeing of Canadians. The pricing framework must respect this premise and not deter early introductions. Furthermore, the review process must be efficient and timely, not duplicative and prolonged due to redundant and overlapping administrative mandates. Patients must not be forced to endure extended wait times, in some cases over several years, to access new or improved medicines.

It is the BMC's position that if there is not sufficient clarity on impact on patient care and on system efficiency, value and sustainability reforms must be halted until there is full certainty.

In addition, officials and decision makers must carefully and meaningfully consider the full scope of input and policy options presented by all stakeholders, including the pharmaceutical industry, the broader life sciences community, public and private payers, and health care professionals. Along with patients, individuals and groups from each of these communities are well equipped to provide informed perspectives and expertise and have a legitimate role in determining the next iteration of a pharmaceutical pricing regulation framework, and therefore should be fully engaged.

## ***Proposed Amendments: Issue Review And Discussion***

Pharmaceutical pricing is complex with diverse implications for pharmaceutical industry profitability and investments, the Canadian research and innovative infrastructure, and the economy broadly. These implications are significant, and ultimately have downstream impact on the healthcare system and patient care and so warrant full consideration. However, the BMC is primarily focussed on issues with a direct connection to patient care.

From a patient perspective, in reviewing the proposed draft amendments, the following issues are considered critical:

### ***Availability: Pharmaceutical Introductions Into Canadian Market***

From our review, there are worrisome indications that Canada is at risk of losing ground in terms of the scope of medicines introduced, compared to other countries, should the proposed regulations be implemented. The realistic possibility of this unintended consequence must be fully understood and addressed.

By many estimations, including the PMBRB's own *Med Entry Watch Report*, 2015, Canada is currently among leading countries within the OECD in terms of percentages of all new drugs globally which are launched here. In examining this report, it can be surmised that Canada would no longer be in the preferred tier as it moves towards pricing in line with OECD median pricing, as proposed, where there are fewer or delayed launches of new/improved drugs.

It is worrisome to consider what impact the proposed regime will have on decisions by global pharmaceutical manufacturers such as how many, when, and which new/improved drugs to launch into the Canadian market. While this is difficult for patient communities to evaluate, the pharmaceutical industry cautions that due to price, process and unpredictability, Canada could be de-prioritized for new drug launches.

***PMPRB comparator countries.*** While certainly there are various aspects to consider, analysis indicates that those countries with lower price ceilings are faced with later or fewer pharmaceutical introductions. A careful reconsideration of the proposed PMPRB price comparator countries is warranted.

The draft regulations propose to remove the USA and Switzerland from the list of price comparators and replace them with Australia, Belgium, Japan, the Netherlands, Norway, South Korea and Spain. If PMPRB is correct in stating that the new list of comparators will likely mean a reduction in the median price of drugs in Canada of about 20 per cent, then it is perhaps foolhardy to assume there will be no unintended or unanticipated consequences for patients in terms of access. PMPRB's own data from the 2015 Med Entry Watch Report shows that in Australia and South Korea, only 65 per cent and 54 per cent (respectively) of new drugs launched globally were available. These facts are worrisome for patients.

This issue is of vital importance to current patients with unmet or poorly-met needs, as well as future patients who could benefit from the introduction and availability of medications that are yet to be discovered. Canadian patients with life-threating, debilitating or difficult to treat diseases expect to have access to the same treatments as patients in other advanced countries. We believe that Canadian officials and decision makers have an obligation to make certain that timely availability is not eroded, and therefore ask that the federal government *not* proceed until this has been publicly assessed and fully resolved.

***Clinical trial access.*** Many patients volunteer for and rely on access to clinical trials as an avenue to much-needed treatments prior to Canadian approvals. A complex mix of factors determine whether these trials will be held in a country, including level of quality care, research expertise and infrastructure which is closely related to pharmaceutical investments. Canada's status as a worthy centre for trials must not be compromised as an unintended side effect of drug pricing re-regulation. The list of comparators should not include any jurisdictions which have less access to clinical trials than Canadians have at present because, we reiterate, clinical trials are vital to patients with unmet needs.

***Timely Access: Delayed Introductions and Regulatory Processes***

Under the current regulatory structure, Canada currently benefits from early launches of new pharmaceuticals compared to other countries, including several of those countries in the proposed additions to the PMPRB "basket" of comparators. Again, the Canadian pharmaceutical industry has expressed concerns that this situation could change under a more restrictive regulatory regime. For patients with critical illnesses awaiting treatments, and for all future patients for whom medicines have yet to be discovered, this is a critical issue. Officials and decision makers must work cooperatively with the pharmaceutical industry to understand and assess risks and develop solutions. If there is a chance that the regulatory changes will increase the likelihood that companies will move Canada down their list of countries when they market a new drug, this must be addressed.

***Extended review times.*** Also related to timely access, care must be taken to ensure that a more complicated regulatory process does not result in extending the entire review process, encompassing the time between when a pharmaceutical is initially submitted for approval and when decisions are made on reimbursement.

In the current system, patient groups identify wait times for treatment as a significant barrier to patient care, and policy makers must be diligent in not adding additional steps or redundancies to approval processes. It is appropriate that a pharmaceutical pricing framework be implemented by a national body, and that it operates in concert with and reflect the realities of other national and regional bodies which play a role in pricing, thereby avoiding duplication. For example, implications of the regulations on the role and effectiveness of the panCanadian Pharmaceutical Alliance (pCPA) must be understood to ensure that its effectiveness in managing prices through negotiations is not compromised.

***Role of duplication in delays.*** Currently, pharmaceutical regulatory and program delivery frameworks are often described as convoluted and duplicative, a labyrinth which is itself a barrier to timely access to necessary care. This situation must not be exacerbated and must be improved. Quite simply, patients need the right drug at the right time and the current system falls considerably short of this. There is reason to believe that these proposed regulatory changes will further complicate systems and contribute to delays with no benefit in terms of patient care and outcomes.

Patients are concerned about the duplication and overlap of administrative responsibilities among Health Canada, PMPRB, the Canadian Agency for Drugs and Technology in Health (CADTH), Institut national d'excellence en santé et en services sociaux (INNESS), and the pCPA. The proposal to expand the work of PMPRB to include a cost-effectiveness test, and to elevate this test to special status within the draft regulations, would take PMPRB beyond its original scope of protecting consumers from excessive pricing. Essentially, it would be duplicating the work of assessing, and then negotiating, the value of medicines of established and publicly-funded organizations such as: CADTH/INNESS and pCPA. Canadians do not need another taxpayer-funded organization examining cost effectiveness; we need the existing organizations to do a better and faster job of negotiating value arrangements with pharmaceutical companies.

Furthermore, the proposed PMPRB regulation changes allow no room for patient input into the matter of value or cost-effectiveness. PMPRB needs to develop a meaningful, ongoing patient input process to be in step with current practice.

***Conclusion: Moving Forward***

The PMPRB is not just a body to protect from excessive pricing, but it also has a broad role, along with other bodies, of contributing to an improved health care system. Specifically, to be an effective and relevant part of the entire framework, the PMPRB must play a positive role in maintaining and enhancing a high level of quality care and contributing to improved outcomes for all patients. Pharmaceutical spending is generally viewed as a cost to the system, but there must also be a recognition that it is an investment in the lives of Canadians through reduction of suffering and improved health.

In addition, introducing greater system-wide efficiency, including alignment and avoidance of duplication and overlap, must also be considered goals of this specific regulatory initiative and indeed broader reform. In this context, the pricing regulation package as drafted can be evaluated by asking these questions:

- Does it ultimately contribute to improved patient care and outcomes?

- Does it reduce duplication, improve efficiency, and contribute to value and sustainability of the health care system?

At this juncture, following review and discussion, it is the position of the BMC that there is not sufficient clarity and understanding of all implications to definitively answer yes to the above questions. It is unwise to think that a 20 per cent reduction in the median price of medicines is achievable, without any negative impact on patients. There is a demonstrable risk that patient care will be diminished, not improved, and that aspects of the proposed framework are duplicative and redundant. Therefore, it is the position of the BMC that immediate changes to the Patented Medicines Regulations, as drafted, should not be implemented. Further analysis, meaningful discussion and consultation is required. An appropriate balance must be found so that levels of patient care are improved, and not compromised.

In addition, we urge ongoing monitoring of pricing regulation and a rigorous evaluation of outcomes. This must include full understanding of patient impact, analysis of real savings, and analysis and evaluation of how savings are invested in improved patient care. Patient values and perspectives must be incorporated throughout monitoring and evaluation, including consideration of impact on timely access, availability of a range of treatment options, and system efficiencies such as alignment and reduction of duplication.

BEST MEDICINES COALITION

***About the Best Medicines Coalition***

The Best Medicines Coalition is a national alliance of patient organizations with a shared mission of equitable and consistent access for all Canadians to safe and effective medicines that improve patient outcomes. Areas of interest include drug approval, assessment and reimbursement issues, as well as patient safety and supply concerns. The BMC strives to ensure that Canadian patients have a voice and are meaningful participants in health policy development, specifically regarding pharmaceutical care. The BMC's standing goals are as follows:

- Drug programs which deliver high standards of equitable and consistent access to medications for all Canadians.
- Drug review and post-marketing surveillance systems to address patient safety; knowledge of risks and benefits throughout drug lifecycle.
- Effective models for meaningful and equitable patient participation in drug reviews and policy development.

Through issue education, consensus building, planning and advocacy, patient-driven positions are communicated to decision makers and stakeholders. Formed in 2002 as a grassroots alliance, the BMC was registered under the Not-for-profit Corporations Act in 2012 and is governed by a Board of Directors elected from member organizations.

***Best Medicines Coalition Members***

Alliance for Access to Psychiatric Medication
Arthritis Consumer Experts
Asthma Canada
Better Pharmacare Coalition
Brain Tumour Foundation of Canada
Canadian Arthritis Patient Alliance
Canadian Breast Cancer Network
Canadian Council of the Blind
Canadian Epilepsy Alliance
Canadian Hemophilia Society
Canadian PKU & Allied Disorders
Canadian Psoriasis Network
Canadian Skin Patient Alliance
Canadian Society of Intestinal Research
Canadian Spondylitis Association
Canadian Treatment Action Council
Crohn's & Colitis Canada
Foundation Fighting Blindness
Gastrointestinal Society
Health Coalition of Alberta
Kidney Cancer Canada
Lymphoma Canada
Ovarian Cancer Canada
Parkinson Canada

December 5, 2018

Dr. Mitchell Levine
Chairperson
Patented Medicines Prices Review Board
levinem@mcmaster.ca

Karen Reynolds
Executive Director
Office of Pharmaceuticals Management Strategies
Strategic Policy Branch
Health Canada
karen.reynolds@canada.ca

Dear Dr. Levine and Ms. Reynolds,

I am writing you on behalf of the Best Medicines Coalition (BMC), an alliance of 26 patient organizations with a shared mission of ensuring equitable and consistent access to safe and effective medicines that improve patient outcomes. The PMPRB invited the BMC to appoint a representative to the PMPRB Steering Committee on Modernization of Price Review Process Guidelines, and the BMC put my name forward. I welcomed this opportunity to reinforce BMC's support for a strong, balanced, and fair pricing regulatory framework aimed at sustaining the life, health, and wellbeing of patients, a position clearly stated in our February 14, 2018 submission to Health Canada regarding the proposed amendments.

I was dismayed, as were my BMC patient group colleagues, to read a CBC Second Opinion piece from Kelly Crowe, posted online November 24, 2018, which included quotes attributed to PMPRB executive director, Douglas Clark. I agree with the points expressed in the November 28, 2018 letter that my patient group colleagues, Durhane Wong-Rieger, Canadian Organization for Rare Disorders, and Martine Elias, Myeloma Canada sent to you, along with all members of the Steering Committee. Like them, I found the substance and tone of these quotes attributed to Mr. Clark to be disheartening, and certainly not respectful of the integrity and thoughtfulness that I have endeavored to bring to my volunteer work on the steering committee.

Importantly, I was particularly disturbed that Mr. Clark, as a senior official in a leadership position of an important public body such as the PMPRB, would share his perspectives on Steering Committee deliberations in a public forum. From our perspective, the content of Mr. Clark's comments, assuming he was correctly quoted, was disrespectful. It left the incorrect impression that patient groups and their representatives are not interacting independently and with integrity. Furthermore, Mr. Clark's open sharing is a demonstration of direct and blatant disregard for the conditions of confidentiality stated in the Steering Committee Terms of Reference and the agreement on Chatham House Rules for all comments and positions expressed in meetings.

Given the seriousness of this situation, I request an immediate response to the following: What steps have Health Canada and PMPRB taken to review communications that lead to the online article and what measures are planned to fully address this situation, including disciplinary measures and outreach to those involved? I look forward to your prompt response before the next Steering Committee meeting planned for December 13 in Ottawa.

PMPRB's work to ensure appropriate pricing, including the current modernization effort, is of utmost importance and we reiterate our support for a **fair and balanced framework that protects patients and ensures the best possible care**. We look forward to continuing our work in cooperation with Health Canada, the PMPRB, and all stakeholders to ensure that patient outcomes are a primary concern as policy is deliberated, reviewed, and implemented.

Yours sincerely,

Gail Attara
President & Chief Executive Officer, Gastrointestinal Society
Board of Directors (Past Chair), Best Medicines Coalition

cc: Douglas Clark, Executive Director, PMPRB
Simon Kennedy, Deputy Minister, Health Canada
PMPRB Steering Committee Members
Paulette Eddy, Executive Director, Best Medicines Coalition
Best Medicines Coalition Board of Directors

BEST MEDICINES COALITION

April 5, 2019

**Patented Medicines Prices Review Board**
333 Laurier Avenue West, Suite 1400
Ottawa, ON K1P 1C1

Response to *Questionnaire for the Steering Committee on Modernization of the Price Review Process Guidelines*

Thank you for including representation from three patient groups on the steering committee regarding modernization of the PMPRB. As you know, I am here on behalf of the 27 patient groups that make up the BMC.

The BMC will not be answering the questions posed because most of them are not relevant to the expertise of patient groups. We are not experts in the detailed workings of the pharmaceutical market and the downstream impact of each aspect of the proposed regulations. Furthermore, the hypothetical nature of the questions feels as if it is somewhat of a futile exercise, rather than a true evidence-based process. There are simply too many uncertainties. **What we do have is a solid understanding of the patient experience and know unquestionably that when patients don't get necessary medicines, their health is negatively affected.**

The bottom line is we need effective and safe medications widely available in Canada for patients. We need these medicines to treat genetic anomalies, injuries, diseases, disorders, infections, and other human processes. Anything regulatory or otherwise that impedes, slows, or stops the flow of new or improved medications to Canadians must be viewed with a great deal of caution. If something inhibits this process, then we have a serious problem. Don't let the PMPRB modernization become a serious problem.

Our member groups put a lot of thought and discussion into our formal submission to the process early last year and, as a reminder, it is attached to the email through which this letter reaches you. We stand by our core position that Canada needs balanced regulations that address pricing issues but do not deter or delay the timely introduction of new or improved drugs. We firmly believe that unless there is full confidence that this can be achieved, the work is incomplete.

We take this opportunity to point out that process around the deliberations of the steering committee have been challenging, perhaps to its detriment. We were greatly troubled by a process issue when some of the patient group interactions were inappropriately discussed out of context in the media late last year. Our letter regarding that is also attached, for the record.

The webinar during which the Technical Working Group (TWG) presentation was rushed, unclear, and suffered technical challenges was frustrating to all. This made us feel as if we are simply being processed. We are also disappointed that the only patient representative on the TWG thought it necessary to submit a dissenting report about the lost opportunity to have an authentic consultation.

Unfortunately, the nature of this questionnaire and of the webinar on the TWG report do not provide us with the evidence of an authentic consultation process at the Steering Committee level to date. PMPRB's work to ensure appropriate pricing, within its legal authority, including the current modernization effort, is of utmost importance and we reiterate our support for a fair and balanced framework that protects patients and ensures access to the best possible care and treatments.

We urge you to give full and careful consideration to all input from steering committee members, including that provided by other patient groups, whose positions we support.

Yours sincerely,

Gail Attara

Gail Attara
PMPRB Steering Committee Member
Board Member, Best Medicines Coalition
Chief Executive Officer, Gastrointestinal Society

Attached: 2018-12-05 BMC letter to PMPRB.PDF; 2018-02-14 BMC-PMPRB Regulations Submission.PDF

**From:** Adams, Owen <owen.adams@cma.ca>
**Sent:** April 7, 2019 8:52 AM
**To:** Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
**Cc:** Adams, Owen <owen.adams@cma.ca>
**Subject:** RE: Next Steps for Steering Committee on Modernization of Price Review Process Guidelines

Dear Tanya:
As requested I have completed the questionnaire as best I am able – not being a health economist or clinician – I must emphasize that these are my own views and do not represent those of the Canadian Medical Association. They have not been vetted by anyone. Sincerely, Owen

---

**From:** Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
**Sent:** Wednesday, March 20, 2019 3:24 PM
**To:** Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; sfrank@clhia.ca; jim@canadiangenerics.ca; jody@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; pfralick@imc-mnc.ca; dhamill@imc-mnc.ca; durhane@optimizinghealth.org; durhane@sympatico.ca; Blackmer, Jeff <Jeff.Blackmer@cma.ca>; Adams, Owen <owen.adams@cma.ca>; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; gail@badgut.org; melias@myeloma.ca; Doidge, Scott: HC <scott.doidge@hc-sc.gc.ca>; susan.pierce@canada.ca
**Cc:** Brittany.Nagy@ontario.ca; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow <RoxanneB@cadth.ca>; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; gfreund@imc-mnc.ca; Christina@canadiangenerics.ca; pclement@imc-mnc.ca; Clark, Karen <Karen.Clark@cma.ca>; megan.steen@canada.ca; ryan.redecopp@canada.ca; Guillaume Couillard <guillaume.couillard@pmprb-cepmb.gc.ca>; Elena Lungu <elena.lungu@pmprb-cepmb.gc.ca>; Richard Lemay <richard.lemay@pmprb-cepmb.gc.ca>; Linda Payant <linda.payant@pmprb-cepmb.gc.ca>; Isabelle Demers <isabelle.demers@pmprb-cepmb.gc.ca>; Murielle Marie <murielle.marie@pmprb-cepmb.gc.ca>; Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>; Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca>; Isabel Jaen Raasch <isabel.jaenraasch@pmprb-cepmb.gc.ca>; Matthew Kellison <matthew.kellison@pmprb-cepmb.gc.ca>; Theresa Morrison <Theresa.Morrison@pmprb-cepmb.gc.ca>
**Subject:** [Sender Auth Failure] Next Steps for Steering Committee on Modernization of Price Review Process Guidelines
**Importance:** High

Dear Steering Committee Members,

In preparation for our last meeting please find attached a word document which contains all the questions that have been posed for the SC as part of the consultation process.

We introduced the proposed questions at our first face-to-face meeting June 25th , along with the proposed new PMPRB Guidelines Framework. Subsequent meetings focused on identifying possible topics for the Technical Working Group (TWG) as well as unpacking each aspect of the proposed framework and soliciting feedback. At our meeting in December, hypothetical case studies were presented in order to demonstrate how the framework could work in practice and provided an assessment of current guidelines relative to the proposed ones. Most recently, the SC received a copy of the Final Technical Working Group Report and the chair, Dr. M. Paulden, provided a webcast on the recommendations. We would like to offer the SC an additional opportunity to ask any follow up or clarifying questions on the TWG report. As has been the practice with feedback, please ensure to pose the questions with a cc to the entire SC before **March 29th**. Attached for your benefit is a copy of the presentation from the webcast.

We kindly ask you to provide your final formal feedback to the specific questions that had been identified by Board Staff on the attached questionnaire. Your responses along with other feedback that has already been received will be reflected in the final Steering Committee Draft report which we will circulate in advance of our next meeting. Steering Committee members will be provided with an opportunity to review the draft and ensure that we have accurately captured your feedback in the report. SC members will also be given an opportunity to speak to their feedback at the meeting to ensure everyone can hear the perspective directly.

We ask that you fill out the questionnaire by **April 8th.** We will be following up shortly with a doodle poll to see what dates work best for SC members in early May.

Sincerely,

**Tanya Potashnik**
Director, Policy and Economics Analysis Branch | Direction des politques et de l'analyse économique
Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés
Box L40, 333 Laurier Avenue West, Suite 1400 | Boîte L40, 333, rue Laurier ouest, Bureau 1400
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Patented Medicine Prices Review Board (PMPRB)

# Questionnaire for the Steering Committee on Modernization of Price Review Process Guidelines

Due date for receiving responses: **COB April 8th, 2019**

## Topic 1: Use of external price referencing (EPR): median international price test (MIPC)

- The proposed approach is that all new medicines are assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).
- The MIPC would be recalculated annually until there are at leasdfast 7 countries or 3 years post first date of sale. At that point the MLP would no longer be interim. This approach provides both predictability (e.g., exchange rate fluctuations) and reduces regulatory burden.
- Re-benching could result in the MLP being adjusted over time.
- IMS will be used to verify international list prices however filing requirements for patentees will remain unchanged for the new schedule.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

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|---|
| Stakeholder input/comments:O Adams – I do not recall much discussion about this at the steering committee (SC) but the rationale for the 12 is set out clearly in the December 2, 2017 proposal. The implications of this can be seen if you look at the most recent OECD data on per capita expenditure on health at US$ parity for 2017. The average for the current 7 countries is $6,021 which is 29% greater than the average of $4,664 for the proposed 12 countries and 51% greater than the OECD average of $3,992 (Canada was $4,826). I personally think that Canada pays a premium in health care spending simply by living next door to the US – although I have never seen any papers that have attempted to quantify it. I think it will be important to have defined criteria for evaluating the outcome of a shift to 12 from the current 7. |

2. **Should exceptions be made to the MLP-MIPC test and, if so, when and why?**

| |
|---|
| Stakeholder input/comments:O Adams – cannot think of any. |

3. **Should there be a price floor for Category 2 medicines based on Lowest International Price Comparison (LIPC)?**

| Stakeholder input/comments:O Adams - that seems reasonable |
|---|

4. **Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?**

| Stakeholder input/comments:O Adams – that seems reasonable |
|---|

5. **Should an increasing gap between MIPC and the MLP trigger a re- bench?**

| Stakeholder input/comments:O Adams – that would seem reasonable |
|---|

6. **Should EPR differ depending on category or vintage of the patented medicine?**

| Stakeholder input/comments:O Adams – sorry could not find this acronym in any of the documents. |
|---|

## Topic 2: Use of List and Net Price Ceilings

- The conceptual framework presented to the SC at the first meeting proposed the establishment of two ceilings for Category 1 medicines based on both list (MLP) and net (rebated) prices (MRP).
- For Category 2 medicines, the proposal is to establish one ceiling (MLP) based on list prices domestically and internationally based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC). No Category 2 medicine will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- The approach aims to establish a net price ceiling to both protect Canada's true transaction price from being exposed and allow patentees to comply with the net price ceilings through use of all discounts/rebates direct and indirect.

## Questions

1. **Should a Category 1 medicine ever have more than one MRP?**

| |
|---|
| Stakeholder input/comments:O Adams – The Tech Working Group unanimously recommended a sinlge price ceiling across all indications I would have no basis to disagree. |

2. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

| |
|---|
| Stakeholder input/comments:O Adams – none have occurred to me. |

3. **Should confidential third party pricing information only be used for compliance purposes?**

| |
|---|
| Stakeholder input/comments:O Adams – I expect this will be a start but I recall discussion from industry reps at the meetings that it is not always feasible to gather that information so that would need to be addressed first. |

## Topic 3: Risk Assessment and Prioritization Criteria for Category 1 & 2 medicines

- The second part of the framework consists of a screening phase which would classify new patented medicines as either high or low priority based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans).
- The framework proposed high level criteria that PMPRB would use to categorize medicines as Category 1 or 2:
    - First in class or substantial improvement over existing medicines for clinically significant indication(s)
    - Market Size >Affordability Threshold
    - ICER > maximum opportunity cost threshold

  - Annual or treatment cost> per capita GDP
- Medicines that appear to be high priority based on these screening factors would be subject to automatic investigation and a comprehensive review to determine whether their price is potentially excessive.

## Questions

1. **Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?**

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| Stakeholder input/comments:O Adams – this seems reasonable |

2. **Should further categories exist with different treatment modalities?**

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| Stakeholder input/comments:O Adams – none to suggest |

3. **Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?**

| |
|---|
| Stakeholder input/comments:O Adams – Tech Working Group unanimously voted not to recommend additional criteria – hence I would agree |

4. **Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?**

| |
|---|
| Stakeholder input/comments:O Adams – the Tech Working Group voted 10 to 2 in favour of PMPRB should set a threshold for each of these factors – hence agree |

5. **Should Category 2 medicines be scrutinized more or less than proposed?**

| |
|---|
| Stakeholder input/comments:O Adams – not sure what the specific proposal is. |

## Topic 4: Re-Benching Criteria

- All new medicines will be given an interim MLP of 3 years or until the medicine is sold in 7 countries, whichever comes first.
- MLP is then frozen, as is MRP, unless re-benching is triggered by one of the following criteria:
    - Approval of a new indication
    - Sales in excess of expected market size
    - New evidence on cost-effectiveness (e.g. CADTH therapeutic class review or lifting of HC conditions on NOC)
    - Significant changes in international prices (eg. MIPC < MIPC at intro by more than 25%)
- Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI
- Complaints received by the PMPRB will trigger an investigation, during which the PMPRB will assess whether:
    - The medicine is in compliance with the Guidelines; and
    - Whether circumstances in the market have changed to warrant a re-benching/reclassification.

### Question

1. **How often and in what circumstances should a medicine be re-benched?**

| |
|---|
| Stakeholder input/comments:O Adams – the triggering circumstances outlined above seem reasonable – on an as needed basis. |

## Topic 5: Tests for Category 1 Medicines

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).
- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

## Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

| Stakeholder input/comments:O Adams see Q1 under topic 1 |
|---|

2. **Should exceptions be made to the MIPC test and, if so, when and why?**

| Stakeholder input/comments:O adams see Q2 under topic 1 |
|---|

3. **Should the cost effectiveness threshold for Category 1 drugs vary?**

| Stakeholder input/comments:O Adams – I agree with Tech Working Group recommendation 2.8 that PMPRB needs to do further empirical research on this issue |
|---|

4. **Should a Category 1 medicine ever have more than one MRP?**

| Stakeholder input/comments:O Adams – see Q1 under Topic 2 |
|---|

5. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

| Stakeholder input/comments:O Adams – none I can think of |
|---|

## Topic 6: Tests for Category 2 Medicines

- Category 2 medicines have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).

- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex- factory) prices, domestically and internationally.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?**

| Stakeholder input/comments:O Adams See Q1 under Topic 1 |
|---|

2. **Should exceptions be made to the MIPC test and, if so, when and why?**

| Stakeholder input/comments:O Adams See Q2 under Topic 1 |
|---|

3. **Should there be a price floor for Category 2 drugs and, if so, should it be based on LIPC?**

| Stakeholder input/comments:See Q3 under Topic 1 |
|---|

4. **Should Category 2 drugs be scrutinized more or less than proposed?**

| Stakeholder input/comments:O Adams – not sure what the specific proposal is |
|---|

## Topic 7: Use of Confidential Pricing Information

- Price reviews would be conducted for the following customer classes:
  - National/Provincial Retail – list price assessed against MLP
  - National Private Payer – ATP assessed against MRP
  - Provincial Public Payer – ATP assessed against MRP in each market

- ATPs are calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

### Questions

1. **Are the proposed definitions of markets and customer classes reasonable?**

| Stakeholder input/comments:O Adams – I am not an expert but wonder if you need to distinguish between public drug programs and public hospital drug purchasing |
|---|

2. **Is the proposal to use third-party pricing information for compliance with the MRP reasonable?**

| Stakeholder input/comments:O Adams – assuming that it is feasible to accurately compile this information. |
|---|

## Topic 8: Application of New Regime to Existing Medicines

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 drugs would be re-benched later unless a complaint is received.
- All drugs within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to come into compliance.

### Questions

1. **Is the use of MIPC as an interim ceiling reasonable?**

| Stakeholder input/comments:O Adams – seems logical |
|---|

2. **Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?**

| |
|---|
| Stakeholder input/comments:O Adams – perhaps only Category 1 |

3. **Are there reasonable alternative approaches to bringing existing medicines under the new framework?**

| |
|---|
| Stakeholder input/comments:O Adams – cannot think of any |

## General Question

**Are there any other questions or comments that you would like to share with the SC that have not been captured above?**

| |
|---|
| Stakeholder input/comments:O Adams – overall I have to wonder about the choice of a supply-side CE threshold – I reviewed the Ochalek and Bokhari papers -however the weight of the literature on whether health is a luxury or normal good suggests that it is a normal good so that may not be an unrealistic approach. |

| | |
|---|---|
| **From:** | Declan Hamill |
| **To:** | Tanya Potashnik |
| **Cc:** | Brittany.Nagy@ontario.ca; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; Christina@canadiangenerics.ca; Pascale Clement; Clark, Karen; megan.steen@canada.ca; ryan.redecopp@canada.ca; Guillaume Couillard; Elena Lungu; Richard Lemay; Linda Payant; Isabelle Demers; Murielle Marie; Claudia Lacroix; Isabel Jaen Raasch; Matthew Kellison; Theresa Morrison; Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; sfrank@clhia.ca; jim@canadiangenerics.ca; jody@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; Pamela Fralick; durhane@optimizinghealth.org; durhane@sympatico.ca; Blackmer, Jeff; Adams, Owen; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; gail@badgut.org; melias@myeloma.ca; Doidge, Scott: HC; susan.pierce@canada.ca; Michael Dietrich |
| **Subject:** | RE: Next Steps for Steering Committee on Modernization of Price Review Process Guidelines |
| **Date:** | Monday, April 8, 2019 11:26:29 AM |

Dear Tanya:

Further to our email sent on March 29, 2019 outlining our questions regarding the Technical Working Group (TWG) process and reiterating our previous concerns with the Steering Committee (SC) process, this message serves to complete our response to your email request dated March 20, 2019.

On behalf of Innovative Medicines Canada (IMC), we note that the questions posed by PMPRB staff are based on the assumption that the proposed regulatory amendments will be enacted as pre-published in Canada Gazette Part I, December 2017.

We remain of the view that the proposed new economic factors and reporting requirements are beyond the jurisdiction of the PMPRB and are not practical to implement within its current quasi-judicial regime. Consequently, and since the proposed regulatory amendments have not been finally published as of the date of this response, we do not believe that it is reasonable or appropriate to require answers to such detailed questions pertaining to the complex implementation of changes that are not yet approved, and that our membership strongly opposes.

Despite this and our view that the TWG and SC consultation processes are out of the traditional and appropriate sequence following the approval of the associated regulatory amendments, we have made good faith efforts to engage in the SC process. Unfortunately, the evolution of the SC process has validated our initial concerns that it is not a venue for meaningful consultation or stakeholder engagement.

In addition, we note that the questions posed are of a highly technical nature and have been posed to SC members, some of whom have either limited or no pricing regulation expertise. This places SC members in a difficult position and casts doubt on the utility of any responses to the questionnaire. In our view, the questionnaire should not be used as a basis for an SC Report.

Further, we note that the committee has not been engaged to date in a discussion on the eventual SC Report or its potential content. In our view, there has been insufficient discussion at the Steering Committee level to justify the production of an SC Report to the PMPRB's Board.

If a report is eventually produced by PMPRB staff for the PMPRB Board, we request that additional time and opportunity be provided to comment on it, and that these comments and previous industry comments be noted 'on the record', consistent with the practice adopted at the TWG.

Thank you and please contact me if there are any questions.

Sincerely,

Declan Hamill

**DECLAN HAMILL**

*Vice-President, Legal, Regulatory Affairs & Compliance | Vice-Président, Affaires juridiques et réglementaires, et Conformité*

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**From:** Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
**Sent:** March-20-19 3:24 PM
**To:** Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; sfrank@clhia.ca; jim@canadiangenerics.ca; jody@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; Pamela Fralick <pfralick@imc-mnc.ca>; Declan Hamill <dhamill@imc-mnc.ca>; durhane@optimizinghealth.org; durhane@sympatico.ca; Blackmer, Jeff <Jeff.Blackmer@cma.ca>; Adams, Owen <owen.adams@cma.ca>; gdoucet@pharmacists.ca; jwalker@pharmacists.ca; gail@badgut.org; melias@myeloma.ca; Doidge, Scott: HC <scott.doidge@hc-sc.gc.ca>; susan.pierce@canada.ca
**Cc:** Brittany.Nagy@ontario.ca; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow <RoxanneB@cadth.ca>; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; Gesine Freund <gfreund@imc-mnc.ca>; Christina@canadiangenerics.ca; Pascale Clement <pclement@imc-mnc.ca>; Clark, Karen <Karen.Clark@cma.ca>; megan.steen@canada.ca; ryan.redecopp@canada.ca; Guillaume Couillard <guillaume.couillard@pmprb-cepmb.gc.ca>; Elena Lungu <elena.lungu@pmprb-cepmb.gc.ca>; Richard Lemay <richard.lemay@pmprb-cepmb.gc.ca>; Linda Payant <linda.payant@pmprb-cepmb.gc.ca>; Isabelle Demers <isabelle.demers@pmprb-cepmb.gc.ca>; Murielle Marie <murielle.marie@pmprb-cepmb.gc.ca>; Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>; Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca>; Isabel Jaen Raasch <isabel.jaenraasch@pmprb-cepmb.gc.ca>; Matthew Kellison <matthew.kellison@pmprb-cepmb.gc.ca>; Theresa Morrison <Theresa.Morrison@pmprb-cepmb.gc.ca>
**Subject:** Next Steps for Steering Committee on Modernization of Price Review Process Guidelines
**Importance:** High

Dear Steering Committee Members,

In preparation for our last meeting please find attached a word document which contains all the questions that have been posed for the SC as part of the consultation process.

We introduced the proposed questions at our first face-to-face meeting June 25th , along with the proposed new PMPRB Guidelines Framework. Subsequent meetings focused on identifying possible topics for the Technical Working Group (TWG) as well as unpacking each aspect of the proposed framework and soliciting feedback. At our meeting in December, hypothetical case studies were presented in order to demonstrate how the framework could work in practice and provided an assessment of current guidelines relative to the proposed ones. Most recently, the SC received a copy of the Final Technical Working Group Report and the chair, Dr. M. Paulden, provided a webcast on the recommendations. We would like to offer the SC an additional opportunity to ask any follow up or clarifying questions on the TWG report. As has been the practice with feedback, please ensure to pose the questions with a cc to the entire SC before **March 29th**. Attached for your benefit is a copy of the presentation from the webcast.

We kindly ask you to provide your final formal feedback to the specific questions that had been identified by Board Staff on the attached questionnaire. Your responses along with other feedback that has already been received will be reflected in the final Steering Committee Draft report which we will circulate in advance of our next meeting. Steering Committee members will be provided with an opportunity to review the draft and ensure that we have accurately captured your feedback in the report. SC members will also be given an opportunity to speak to their feedback at the meeting to ensure everyone can hear the perspective directly.

We ask that you fill out the questionnaire by **April 8th.** We will be following up shortly with a doodle poll to see what dates work best for SC members in early May.

Sincerely,

**Tanya Potashnik**
Director, Policy and Economics Analysis Branch | Direction des politques et de l'analyse économique
Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés
Box L40, 333 Laurier Avenue West, Suite 1400 | Boîte L40, 333, rue Laurier ouest, Bureau 1400
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Government of Canada | Gouvernement du Canada

| | |
|---|---|
| **From:** | Durhane Wong-Rieger |
| **To:** | Tanya Potashnik |
| **Cc:** | Hamill Declan; Nagy Brittany; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; Christina@canadiangenerics.ca; Pascale Clement; Clark, Karen; megan.steen@canada.ca; ryan.redecopp@canada.ca; Guillaume Couillard; Elena Lungu; Richard Lemay; Linda Payant; Isabelle Demers; Murielle Marie; Claudia Lacroix; Isabel Jaen Raasch; Matthew Kellison; Theresa Morrison; McGurn Suzanne (MOHLTC); Ali Imran (MOHLTC); Moneo Mitch; michael.sherar@cancercare.on.ca; McLeod Robin; O'Rourke Brian; Boileau Luc; sylvie.bouchard@inesss.qc.ca; Reynolds Karen; Dagenais Eric; Arancibia Rodigo; Frank Stephen; Keon Jim; Cox Jody; Redding Laurene; Petrelli Paul; Fralick Pamela; Blackmer Jeff; Adams, Owen; Doucet Glen; jwalker@pharmacists.ca; Attara Gail; Elias Martine; Doidge, Scott: HC; Pierce Susan; Michael Dietrich |
| **Subject:** | Re: Next Steps for Steering Committee on Modernization of Price Review Process Guidelines |
| **Date:** | Monday, April 8, 2019 11:45:12 AM |
| **Attachments:** | PMPRB letter to PM Trudeau re TWG and PMPRB regs April 8 2019.pdf |

Dear Tanya,

Please find our Open Letter to the Prime Minister on the responses to the PMPRB Steering Committee questions. We are very much in agreement with the views of the other patient member.

Durhane Wong-Rieger
President & CEO
Canadian Organization for Rare Disorders
151 Bloor Street West, Suite 600
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www.raredisorders.ca

> On Apr 8, 2019, at 11:25 AM, Declan Hamill <dhamill@imc-mnc.ca> wrote:
>
> Dear Tanya:
>
> Further to our email sent on March 29, 2019 outlining our questions regarding the Technical Working Group (TWG) process and reiterating our previous concerns with the Steering Committee (SC) process, this message serves to complete our response to your email request dated March 20, 2019.
>
> On behalf of Innovative Medicines Canada (IMC), we note that the questions posed by PMPRB staff are based on the assumption that the proposed regulatory amendments will be enacted as pre-published in Canada Gazette Part I, December 2017.
>
> We remain of the view that the proposed new economic factors and reporting requirements are beyond the jurisdiction of the PMPRB and are not practical to

implement within its current quasi-judicial regime. Consequently, and since the proposed regulatory amendments have not been finally published as of the date of this response, we do not believe that it is reasonable or appropriate to require answers to such detailed questions pertaining to the complex implementation of changes that are not yet approved, and that our membership strongly opposes.

Despite this and our view that the TWG and SC consultation processes are out of the traditional and appropriate sequence following the approval of the associated regulatory amendments, we have made good faith efforts to engage in the SC process. Unfortunately, the evolution of the SC process has validated our initial concerns that it is not a venue for meaningful consultation or stakeholder engagement.

In addition, we note that the questions posed are of a highly technical nature and have been posed to SC members, some of whom have either limited or no pricing regulation expertise. This places SC members in a difficult position and casts doubt on the utility of any responses to the questionnaire. In our view, the questionnaire should not be used as a basis for an SC Report.

Further, we note that the committee has not been engaged to date in a discussion on the eventual SC Report or its potential content. In our view, there has been insufficient discussion at the Steering Committee level to justify the production of an SC Report to the PMPRB's Board.

If a report is eventually produced by PMPRB staff for the PMPRB Board, we request that additional time and opportunity be provided to comment on it, and that these comments and previous industry comments be noted 'on the record', consistent with the practice adopted at the TWG.

Thank you and please contact me if there are any questions.

Sincerely,

Declan Hamill

**DECLAN HAMILL**

*Vice-President, Legal, Regulatory Affairs & Compliance | Vice-Président, Affaires juridiques et réglementaires, et Conformité*

**T** (613) 236 0455, x 425 **C** (613) 301 8794

innovativemedicines.ca | @innovativemeds

---

**From:** Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
**Sent:** March-20-19 3:24 PM
**To:** Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca;

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**Cc:** Brittany.Nagy@ontario.ca; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow <RoxanneB@cadth.ca>; annie.gariepy@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; Gesine Freund <gfreund@imc-mnc.ca>; Christina@canadiangenerics.ca; Pascale Clement <pclement@imc-mnc.ca>; Clark, Karen <Karen.Clark@cma.ca>; megan.steen@canada.ca; ryan.redecopp@canada.ca; Guillaume Couillard <guillaume.couillard@pmprb-cepmb.gc.ca>; Elena Lungu <elena.lungu@pmprb-cepmb.gc.ca>; Richard Lemay <richard.lemay@pmprb-cepmb.gc.ca>; Linda Payant <linda.payant@pmprb-cepmb.gc.ca>; Isabelle Demers <isabelle.demers@pmprb-cepmb.gc.ca>; Murielle Marie <murielle.marie@pmprb-cepmb.gc.ca>; Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>; Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca>; Isabel Jaen Raasch <isabel.jaenraasch@pmprb-cepmb.gc.ca>; Matthew Kellison <matthew.kellison@pmprb-cepmb.gc.ca>; Theresa Morrison <Theresa.Morrison@pmprb-cepmb.gc.ca>
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Sincerely,

**Tanya Potashnik**
Director, Policy and Economics Analysis Branch | Direction des politques et de l'analyse économique
Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés
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Facsimile | Télécopieur 613-952-7626
Government of Canada | Gouvernement du Canada

***VIA EMAIL AND POSTED PUBLICLY***

April 8, 2019

The Right Honourable Justin Trudeau, PC, MP
Prime Minister of Canada
80 Wellington St.
Ottawa, Ontario K1A 0A2

**Subject:** **Patients say "NO" to unjustifiable new regulations that will obstruct the entry of new medicines to Canada**

Dear Prime Minister Trudeau,

We apologize in advance if the tone of this letter conveys less than the utmost respect. What you are actually sensing is our extreme frustration and indeed fear for Canadians who rely on access to patented medicines.

Specifically, we are concerned about your government's proposed changes to the Patented Medicines Regulations, which would overhaul how the Patented Medicine Prices Review Board (PMPRB) sets maximum (non-excessive) prices for patented drugs in Canada.

As two of the three patient members appointed to the PMPRB Steering Committee on Guidelines Modernization (SC), we feel strongly that our responsibility is to ensure the needs of the millions of Canadian patients are adequately reflected in the proposed regulatory changes. Outside of the Steering Committee process, our organizations have also consulted with patients and the public to develop extensive and detailed feedback over the past two years. It is not an overstatement to say that *none* of our input has been addressed or resulted in any substantive changes in the Health Canada and PMPRB proposals.

The Steering Committee process has been even more frustrating and ultimately infuriating. As patient members, we have had to work diligently to understand the potential impact of proposed changes, to actively participate in the Steering Committee discussions, and to provide oral and written input.

It was clear from the start that none of the SC members had any real role in steering guidelines development. Instead, we were limited to responding to policy directions already decided by PMPRB staff. They provided limited information (data and analyses) to validate the policies and guidelines that were presented and they rejected the opportunity to propose any alternatives or options for achieving the ultimate goal (that is, ensuring non-excessive and internationally compatible prices). One can see clearly in each set of meeting minutes and subsequent documents the limited scope of discussions and minimal impact on the original policies and guidelines.

The experience with the Technical Working Group (TWG), set up to provide scientific and economic rationale for the proposed regulations and criteria for implementation has been equally if not more maddening. At the conclusion of their five-to-six-month work, they produced a report that basically said they were unable to substantiate the premises for the PMPRB guidelines. They were also unable to make any recommendations for changes, primarily because they did not have access to the necessary information, or they were limited by their terms of reference.

Steering Committee members were presented with these "non-recommendations" by the Chair of the TWG in a one-hour teleconference and then subsequently asked to provide opinions on a series of questions that are essentially unanswerable because we do not have the data or analyses on which to make any informed judgments. We choose not to provide arbitrary answers that will perpetuate the myth that there was ever a Steering Committee. We have been no more than passengers in a vehicle on a pre-set course that is now going "over the cliff" (think: crash test dummies).

In summary, based on what we do know from the case studies prepared by the PMPRB staff, the impact of the proposed regulations will be to drive initial list prices to levels so low (about 30% to 90% below most international list prices) that no company will bring new drugs to Canada. This is not an idle threat; it is just the experience of countries (mostly low- and middle-income ones) that have extremely depressed prices.

We all want to have access to medicines at affordable prices. However, these proposed changes by the PMPRB will mean that many new therapies will not be available in Canada.

**It will be unethical, unjustifiable, and unfair but nevertheless inevitable that Canadian patients will be denied breakthrough, lifesaving, and even incrementally better medicines.**

Instead of responding to the questions, given the lack of real consultations by both Health Canada and the PMPRB staff, we feel compelled to take this opportunity to share our questions and our responses that will explain why the PMPRB reform needs to be fundamentally reconsidered.

***Question 1: What is the impact on patient access to new medicines?***

The proposed new federal regulations would mandate drug prices so low that we are concerned that companies will not launch new drugs in Canada, or they will wait until after they have been available for years, everywhere else.[1]

[1] Steering Committee on Modernization of Price Review Process Guidelines, specifically, the Guideline Modernization: Case Studies and Proposed Application of PE and Market Size Factors to Category 1 Drugs (http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1378&lang=en).

***Question 2: Who is at risk?***

Patients with terminal cancer who have failed all previous therapies; patients with rare conditions who have no previous therapies; patients for whom cell and gene therapy may offer a rescue; and patients with chronic conditions whose current therapies are losing their effectiveness.

***Question 3: Is this unethical?***

The proposed regulations instruct the PMPRB to target those therapies with the greatest unmet need and those that offer potentially the biggest improvement over existing therapies. Moreover, the PMPRB states, "…that its mandate is to protect consumers from excessive pricing, and not to ensure that products are launched into the market."[2]

***Question 4: What is unjustifiable about the proposed reforms?***

The proposed regulations will define how new ceiling prices will be calculated based on a number of factors, mostly economic, but not determined or supported by science, economic analysis, modeling, best practices, or even the experience of other countries. We are not aware of any other country in the world that proposes to regulate both the public list price and confidential price for every transaction in an entire jurisdiction, and outside of a reimbursement or pharmacare program.

***Question 5: Are the "cost-effectiveness" thresholds valid?***

In July 2018, the PMPRB Technical Working Group was set up to validate or recommend changes to the criteria, metrics, and criterion thresholds, along with other cost-effectiveness considerations. The TWG presented its report in March 2019 to the PMPRB and the Steering Committee, and concluded it was mostly unable to validate the PMPRB's proposed criteria and also unable to provide solid recommendations. The TWG cited the lack of "necessary data" to even model how many drugs would be classified for increased scrutiny.[3] The TWG was "unanimous in considering the empirical evidence with respect to Canadian estimates of supply-side thresholds to be uncertain."[4] This uncertainty is compounded by the fact that the only study cited to estimate this threshold was not peer reviewed, the research was not primarily based on Canadian data and some of the variables employed were not relevant to Canada.[5]

In fact, the TWG found that they could not definitively address most of the recommendations posed in their Terms of Reference, citing "limitations in the empirical and theoretical literature."[6]

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[2] Technical Working Group report p. 53.
[3] TWG report p. 18.
[4] TWG report p. 23.
[5] Assessing health opportunity costs for the Canadian health care systems (Report by the University of York) (http://www.pmprb-cepmb.gc.ca/CMFiles/Consultations/new_guidelines/Canada_report_2018-03-14_Final.pdf).
[6] TWG report p. 28.

In the 52-page TWG Final Report, the words "uncertain" or "uncertainty" are used in reference to the evidence, analyses, findings, and/or recommendations exactly 100 times.

***Question 6: Why are the proposed regulations unfair?***

The predominantly economic criteria, however inexact, will be applied equally across all therapies without regard for disease severity, rarity, treatment options, or other factors.

Indeed, the TWG recognized that there should be equity weights applied but did not have the information (knowledge base) to do so. "Characteristics that are often found to be important in empirical studies include severity of illness (particularly the presence or otherwise of life threatening or progressively chronically debilitating illness), the availability of active treatment alternatives, the prevalence of disease, the type of health gain (such as a reduction in pain), and the magnitude of health gain. These factors are often found to interact with one another, and so should not be considered independently. In the opinion of this member, greater empirical work is needed to fully understand these interactions and the 'weights' that would be put on each characteristic." [7] However, the TWG could not make a recommendation as to how equity weights could be implemented due to "limitations in the existing theoretical and empirical evidence base."[8]

That means, all other things being equal, the "maximum allowed cost" to provide "one additional year of life" for (1) a six-year-old with progressive neuromuscular disease, (2) a 42-year-old with metastatic breast cancer, and (3) an 81-year-old with well-controlled Type 2 diabetes is exactly the same. You can guess which medicines will meet the Canadian price threshold, and which will not.

***Question 7: Will the proposed regulations and the subsequent "ceiling price setting" result in lower Canadian prices for new medicines?***

The proposed switch in the basket of reference countries, including the dropping of the highest public price comparators (USA and Switzerland) and inclusion of lower-price countries could, in fact, result in lower public list prices. That means any payer or consumer purchasing at list price may get a lower transparent price.

However, we have no good analyses or data that can predict the potential impact of these changes on net prices overall. It may make no difference to all other payers who currently negotiate starting from a list price based on a cost-effectiveness assessment.

Even if the starting price were lower, there are no models to suggest that the final negotiated price would be different, especially since the public funders are negotiating collectively. The negotiated prices are confidential and may include risk-sharing agreements, rebates, and patient

[7] TWG report p. 28.
[8] TWG report p. 29.

support programs. Private payers and their plan sponsors who don't negotiate prices may benefit with a lower list price.

What will be different with this proposal is to use the net confidential prices to determine maximum prices for subsequent competitors and to apply that information to re-benching of therapeutic classes. Because every other country follows the current practice of holding negotiated prices confidential, Canada would show a lower list price, and this will inevitably deter companies from coming to Canada until they have negotiated their drug prices elsewhere. So, Canada may not, in the end, pay less than other counties; they will only get their drugs years later than other countries.

***Question 8: Will the proposed regulations result in lower global prices for new medicines?***

There will probably be no impact on global prices unless the rest of the developed world decides to publish their negotiated prices. Transparent pricing, in the long run, is probably a better approach, but Canada cannot go it alone. If we really want changes, we have to work collectively, especially with other OECD countries.

**Question 9: Why are we reforming the PMPRB *and* creating the Canadian Drug Agency**

Finally, your recent Budget announced the creation of a transition office for a new Canadian Drug Agency, which has as one of its objectives, saving Canadians $3 billion annually. The changes to the PMPRB and the Patented Medicines Regulations should be considered in this context. The proposed unfeasible, unfair and unjustified regulations would simply become a barrier to new medicines that the Canadian Drug Agency will rely on to complete the proposed comprehensive formulary.

In summary, we are asking you and your government to reconsider the changes to the Patented Medicines Regulations. Once the regulations are finalized, we are particularly concerned about how the PMPRB – an arm's length agency – will implement the changes. The PMPRB has demonstrated that it intends to implement them in a way that will obstruct and slow patient access to needed medicines.

Given the lack of any real consultations on the PMPRB Guidelines and the Patented Medicines Regulations, we are counting on your leadership to direct your officials to undertake meaningful consultations with patients in the context of your national pharmacare proposal. Done right, consultations on a new national pharmacare program could lead to affordable and appropriate access to medicines that patients need to be well and, in many cases, survive.

Please do not hesitate to reach out to either of us if you require further information regarding our position on this matter.

Sincerely,

Dr. Durhane Wong-Rieger, PhD
President & CEO
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www.myeloma.ca

cc. The Hon. Ginette Petitpas Taylor, PC, MP, Minister of Health
The Hon. Bill Morneau, PC, MP, Minister of Finance
The Hon. Joyce Murray, PC, MP, President of the Treasury Board
Dr. Mitch Levine, Chair, Patented Medicine Prices Review Board
Douglas Clark, Executive Director, Patented Medicine Prices Review Board

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22 May 2019

The Right Honourable Justin Trudeau, PC, MP
Prime Minister of Canada
80 Wellington St.
Ottawa, ON, K1A 0A2

**Subject: Clarifications of the Mandate and Recommendations of the PMPRB 'Working Group'**

Dear Prime Minister,

We are writing in response to an open letter authored by Durhane Wong-Rieger, President & CEO of the Canadian Organization for Rare Disorders (CORD), and Martine Elias, Executive Director of Myeloma Canada, which was emailed to you and posted publicly on 8 April 2019 (*'Patients say "NO" to unjustifiable new regulations that will obstruct the entry of new medicines to Canada'*). This letter is available at *www.raredisorders.ca*.

The authors comment upon a technical 'Working Group' convened by the Patented Medicine Prices Review Board (PMPRB) (formally the *'Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines'*). The Working Group's final report was published by the PMPRB in March 2019 and is available at *www.pmprb-cepmb.gc.ca/view.asp?ccid=1449*.

As the former chair and senior academic members of this Working Group, we would like to clarify a number of material misunderstandings evident in this letter regarding the Working Group's mandate and recommendations. We have provided a detailed clarification for each of these misunderstandings in the attached document.

We believe it is important that policy is made on the basis of an accurate understanding of the technical evidence. We therefore offer these clarifications in the spirit of supporting evidence-based policy development.

Please do not hesitate to reach out to us if you require further clarification on any matters discussed in this letter.

Sincerely,

Dr Mike Paulden, PhD, Assistant Professor, School of Public Health, University of Alberta
Dr Christopher McCabe, PhD, Professor, Department of Emergency Medicine, University of Alberta
Dr Stuart Peacock, DPhil, Professor, Faculty of Health Sciences, Simon Fraser University
Dr Doug Coyle, PhD, Professor, School of Epidemiology and Public Health, University of Ottawa

cc.
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## Clarifications of the Mandate and Recommendations of the PMPRB 'Working Group'

### Mandate of the Working Group

As noted in both the Working Group's report and its Terms of Reference, the mandate of the Working Group was to *"inform the Steering Committee on certain issues that the Steering Committee believed would benefit from the review of experts in health technology assessment and other economic and scientific matters"*.

Critically, as a group of *technical* experts, the purpose of the Working Group was not to comment on the *policy intent* behind the proposed regulations or guidelines. This is made clear throughout the Working Group's report and is reflected in its recommendations.

The authors are therefore incorrect to state that the Working Group was *"set up to provide scientific and economic rationale for the proposed regulations and criteria for implementation"*. The authors are also incorrect to state that the Working Group *"basically said they were unable to substantiate the premises for the PMPRB guidelines"*. Consistent with its mandate, the Working Group took no position on the 'rationale' or 'premises' for the proposed regulations or guidelines. None of the Working Group's recommendations states or implies that the 'premises' for the guidelines were unsubstantiated.

### Recommendations of the Working Group

The Working Group made 23 recommendations, each of which was adopted following a vote of members. Most had unanimous support, and all were supported by at least three quarters of Working Group members.

This broad support for the recommendations reflected the collaborative nature of the Working Group's deliberations. All members had an opportunity to contribute to the Working Group's discussions, to suggest modifications to the draft recommendations, and to propose revisions to the Working Group's draft report prior to submission. The external reviewer noted that *"the guidance and advice offered to the PMPRB seems appropriate and well balanced"*, while the two industry representatives on the Working Group noted that the chair executed his mandate *"as impartially as possible"*.

The Working Group made a number of specific recommendations, including, but not limited to, the following:

- The use of a 'supply-side cost-effectiveness threshold', as a means for estimating the 'opportunity cost' of adopting new medicines within Canada's public health care systems, is consistent with the policy intent;
- Implementing 'equity weights' other than 1 is not recommended at the present time, due to limitations in the existing theoretical and empirical evidence base;
- A single ceiling price should be adopted for each medicine across all indications; and
- All pharmacoeconomic analyses should include an unbiased consideration of uncertainty, in accordance with guidelines published by the Canadian Agency for Drugs and Technologies in Health (CADTH).

The Working Group also recommended specific changes to the PMPRB's proposed criteria for classifying medicines as 'Category 1', including dropping the 'opportunity cost' criterion and considering costs as 'incremental' upon existing treatment (rather than in absolute terms). In light of these recommended changes, the authors are incorrect to state that the Working Group was *"unable to make any recommendations for changes"*.

Some of the Working Group's recommendations were conditional upon the policy intent. For example, the Working Group considered various approaches for setting a single ceiling price for a medicine across multiple indications. Each of these approaches would result in different benefits for patients and manufacturers, as detailed in the Working Group's report, such that determination of the most desirable approach is a matter for policy makers. For this and other 'policy conditional' recommendations, the Working Group report considers a number of *potential* policy objectives, and outlines the set of approaches that is consistent with each objective. Since specifying the *actual* policy objective was not a matter for the Working Group, but rather for policy makers, the Working Group could not and did not recommend any specific approach. Rather, the Working Group

recommended that an approach be adopted that is in line with the policy intent, given the technical considerations made by the Working Group.

Taken together, the Working Group's recommendations sought to provide thoughtful technical guidance to the PMPRB on a range of topics, including risk categorizing medicines, specifying a 'cost-effectiveness threshold', pricing across multiple indications, accounting for uncertainty, and the proposed 'market size adjustment'. These recommendations were made with due respect for the policy intent, and all were supported by a clear majority of Working Group members.

In this context, it is clearly inappropriate for the authors to dismiss the Working Group's findings outright as *"non-recommendations"*. It is particularly regrettable that this dismissal of the Working Group's findings has been made by two members of the PMPRB's Steering Committee, given that the Working Group was commissioned in order to support the Steering Committee's deliberations.

## Responses to the authors' questions

In their letter, the authors propose a number of questions and provide their responses to each. Of these, only questions 4, 5 and 6 pertain to considerations made by the Working Group. Here too, the authors exhibit material misunderstandings of the content of the Working Group's report. We seek to provide clarifications and corrections for these misunderstandings below.

### *Question 4*

In their response to question 4, the authors incorrectly state that the proposed methods for calculating ceiling prices are *"not determined or supported by science, economic analysis, modeling, best practices, or even the experience of other countries"*.

In considering the 'pharmacoeconomic value' factor, the Regulatory Impact Analysis Statement (RIAS) published in Canada Gazette I (Vol. 151, No. 48 - December 2, 2017) states that the PMPRB would consider only those cost-utility analyses prepared by CADTH or the Institut national d'excellence en santé et services sociaux (INESSS). Both organizations conduct economic analyses of new medicines that are supported by modeling, and both organizations publish 'best practice' guidelines on the methods to use for modeling and conducting economic analyses. These guidelines have evolved over time in response to advances in the scientific literature, and share a number of commonalities with 'best practice' guidelines published by established and respected health technology assessment (HTA) agencies in other countries.

### *Question 5*

In their response to question 5, the authors incorrectly state that the Working Group *"concluded it was mostly unable to validate the PMPRB's proposed criteria".*

The Working Group did not make any such conclusion. The authors appear to be referring to section 1.3.6 of the Working Group's report, which focused on the 'threshold' used for each criterion used to classify medicines as Category 1. In this section, the Working Group recommended that *"a threshold for each criterion be determined by the PMPRB, taking into account its capacity for assessing 'Category 1' medicines, the technical considerations of the Working Group, and the policy intent"*.

In its report, the Working Group provided several reasons for why it did not specify a 'threshold' for each criterion. Among these, it noted that specifying thresholds would have implications for the total number of medicines classified as Category 1, and that the Working Group was unaware of the PMPRB's capacity for assessing Category 1 medicines. Furthermore, specifying thresholds across different criteria would have implications for the composition of medicines classified as Category 1; as the report notes, *"the 'ideal' types of medicine to classify as 'high risk' depend upon the policy intent"*. In light of this, a substantial majority of Working Group members agreed that the threshold for each criterion should be specified by the PMPRB, taking into account its capacity for assessing Category 1 medicines, the technical considerations of the Working Group, and the policy intent.

This is very different from concluding that the Working Group was *"mostly unable to validate the PMPRB's proposed criteria"*, as stated by the authors.

Next, the authors incorrectly state that the Working Group was *"unable to provide solid recommendations"*. As noted earlier, the Working Group made 23 recommendations, all supported by a majority of Working Group members, many of which included specific technical advice for the PMPRB.

Later in their response to this question, the authors incorrectly state that the Working Group *"found that they could not definitively address most of the recommendations posed in their Terms of Reference, citing 'limitations in the empirical and theoretical literature'"*.

This quote has been taken out of context. The Working Group's report refers to *"limitations in the empirical and theoretical literature"* only once, in reference to the evidence base around 'equity weights' (one of nine topics considered within the second area of focus). This was cited in only one of the 23 recommendations made by the Working Group, and not in *"most"* recommendations, as implied by the authors.

Context should also be given as to why some recommendations were not 'definitive'. As noted earlier, a minority of recommendations were made conditional upon the policy intent. This was because, in each case, the Working Group identified several potential technical approaches, each with different implications for the benefits that arise to patients and the manufacturers of medicines. Since the desired allocation of the benefits of medicines among patients and manufacturers is a matter for policy makers, the Working Group could not and did not recommend any specific approach. Instead, the Working Group clearly described the implications of each approach and considered which of a number of potential policy objectives would be consistent with each approach. Given this important context, providing recommendations that were conditional upon the policy intent (rather than 'definitive') was not a weakness. Rather, the Working Group respected the differing roles of policy makers and technical experts and made recommendations that enable the PMPRB to make a more informed decision as to which technical approach to adopt in each case, given the policy intent.

The authors conclude their response to this question by noting that, in the Working Group's report, *"the words "uncertain" or "uncertainty" are used in reference to the evidence, analyses, findings, and/or recommendations exactly 100 times"*. This is reflective of the careful consideration given by the Working Group to uncertainty in the evidence base, which is a critical consideration in all high quality pharmacoeconomic analyses.

As noted in the Working Group's report, *"clinical uncertainty is typically the primary source of uncertainty when CADTH considers new medicines, particularly for rare conditions"*. Considerable care must be taken when assessing uncertain clinical evidence, since dismissing evidence regarding the effectiveness of a new medicine on the grounds that it is uncertain can have negative implications for patients. Similar care must also be taken when considering uncertain estimates of the 'supply-side cost-effectiveness threshold', since these estimates are currently the only practical means for estimating the impact that the cost of new medicines has on the health of other patients cared for by Canada's public health care systems. As a result, the Working Group carefully considered the evidence around these thresholds and made a number of thoughtful recommendations. These included a recommendation that the PMPRB support further empirical research, and a recommendation that any 'interim' threshold specified prior to the completion of this research be informed by existing thresholds used by Canadian HTA agencies and estimates of 'supply-side' thresholds from other relevant jurisdictions.

*Question 6*

In their response to question 6, the authors incorrectly state that the Working Group *"recognized that there should be equity weights applied but did not have the information (knowledge base) to do so".*

The Working Group's only recommendation regarding equity weights was that *"[t]he Working Group does not recommend the implementation of 'equity weights' other than 1, as would be required to allow price ceilings above opportunity cost for some medicines but not others, due to limitations in the existing theoretical and empirical evidence base"*. Implementing an equity weight of 1 means that equivalent health gains are valued equally across all patients, and is formally equivalent to applying no weighting at all. Nowhere in the Working Group's report was it *"recognized"* that equity weights other than 1 *"should"* be applied.

The Working Group did not recommend the implementation of equity weights other than 1 for the technical reasons outlined in its report. Hypothetically, if it were technically feasible to apply equity weights other than 1, the question of whether these equity weights *"should"* be applied would then be a normative matter for policy makers to consider (with due regard for the policy intent), and not something for technical experts to 'recognize'.
If applying such equity weights were both technically feasible and desired by policy makers, consideration would need to be made as to the characteristics of the patients who bear the 'opportunity cost' of new medicines through reduced access to other health care services. Applying such equity weights would be expected to cause the ceiling price for some medicines to increase but the ceiling price for other medicines to fall, depending upon the characteristics of patients who benefit from new medicines and the characteristics of those patients whose care will be displaced to pay for the additional cost of new medicines.

The authors conclude their response to this question by stating that *"all other things being equal, the "maximum allowed cost" to provide "one additional year of life" for (1) a six-year-old with progressive neuromuscular disease, (2) a 42-year-old with metastatic breast cancer, and (3) an 81-year-old with well-controlled Type 2 diabetes is exactly the same. You can guess which medicines will meet the Canadian price threshold, and which will not"*.

We are unable to 'guess' the answer to this question because it depends upon a number of factors not considered by the authors. First, it is incorrect to state that *"the 'maximum allowed cost' to provide 'one additional year of life'"* would be the same for each patient, since this ignores any consideration of health-related quality of life.
The primary outcome measure used in economic evaluations conducted by CADTH and INESSS (and many other HTA agencies worldwide) is the 'quality-adjusted life year' (QALY), which takes into account both length of life and health-related quality of life. It follows that a treatment which provides one additional year of life of excellent quality might be associated with a greater QALY gain (and hence a higher *"maximum allowed cost"* under the proposed regulations) than a treatment which provides two additional years of life of poor quality.
Second, the *"maximum allowed cost"* would be dependent upon the *incremental* cost and the *incremental* benefit of the new medicine compared to existing treatment. Even if a new medicine for one patient is less effective than a new medicine for another patient, if the existing treatment for the first patient is worse than that for the second patient then the *incremental* benefit for the first patient might be greater. Similarly, the incremental cost of treatment for each patient depends not only upon the cost of the new medicine but also the cost of existing treatment. Without understanding the cost and benefit of both the existing treatment and the new medicine for each patient (in terms of both length of life *and* health-related quality of life), it is not possible to answer the question posed by the authors.

In summary, the authors' letter reflects a number of fundamental misunderstandings regarding the Working Group's mandate and recommendations. We believe it is important that policy is made on the basis of an accurate understanding of the technical evidence, and we hope that this document has clarified the Working Group's considerations and recommendations on the technical issues that fell within its mandate.

| | |
|---|---|
| **From:** | Stephen Frank |
| **To:** | Tanya Potashnik |
| **Cc:** | adriana.ruiz@cancercare.on.ca; adsa@clhia.ca; amanda.janes@canada.ca; annie.gariepy@inesss.qc.ca; BrianO@cadth.ca; Brittany.Nagy@ontario.ca; celine.makischuk@canada.ca; chantale.beauchamp2@canada.ca; Charlotte.elagab@gov.bc.ca; Christina@canadiangenerics.ca; Claudia Lacroix; dhamill@imc-mnc.ca; durhane@sympatico.ca; durhane@optimizinghealth.org; Elena Lungu; eric.dagenais@canada.ca; gail@badgut.org; gdoucet@pharmacists.ca; gfreund@imc-mnc.ca; Guillaume Couillard; Imran.S.Ali@ontario.ca; Isabelle Demers; Isabel Jaen Raasch; Blackmer, Jeff; jim@canadiangenerics.ca; jody@canadiangenerics.ca; jwalker@pharmacists.ca; Clark, Karen; Karen.reynolds@canada.ca; laurene.redding@astrazeneca.com; Linda Payant; luc.boileau@inesss.qc.ca; Matthew Kellison; megan.steen@canada.ca; melias@myeloma.ca; michael.sherar@cancercare.on.ca; Mitch.Moneo@gov.bc.ca; Murielle Marie; Adams, Owen; Paul.Petrelli@jazzpharma.com; pclement@imc-mnc.ca; pfralick@imc-mnc.ca; Rajni.Vaidyaraj@cancercare.on.ca; Richard Lemay; robin.mcleod@cancercare.on.ca; rodrigo.arancibia@canada.ca; Roxanne Blow; ryan.redecopp@canada.ca; Doidge, Scott: HC; susan.pierce@canada.ca; Suzanne.Mcgurn@ontario.ca; sylvie.bouchard@inesss.qc.ca; Theresa Morrison |
| **Subject:** | Re: Next Steps for Steering Committee on Modernization of Price Review Process Guidelines |
| **Date:** | Tuesday, April 16, 2019 3:23:14 PM |

Dear Tanya:

My apologies for the delayed response to your request below.
I am writing on behalf of the life and health insurance industry to indicate our continued strong support for the modernization framework for the Patented Medicine Prices Review Board (PMPRB).
The PMPRB's role in helping ensure prices in Canada are fair and sustainable for Canadians has never been more important. This is particularly true for Canada's private payers – who collectively reimburse over $11.3 billion per year in drug costs and often bear the burden of list prices on behalf of Canadians.
We continue to believe that patented drug prices in Canada are too high relative to other economies and these added costs are putting enormous strain on the viability of both public and private drug benefit plans.
It has been clear throughout the Steering Committee's deliberations that there are many interests and issues involved in the PMPRB review that contribute to its complexity. However, we believe the proposed framework strikes an appropriate balance that can contribute to an environment conducive to innovation in the pharmaceutical industry, while controlling the costs of prescription drugs for public and private plans, and ultimately Canadians.
For these reasons we believe it is crucial that the government move ahead with the PMPRB modernization framework in the months ahead and resist efforts to revisit the proposed changes at this late stage.
Sincerely,

Stephen

**Stephen Frank**
President and CEO
Direct: 416-359-2965
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From: Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
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Date: 03/20/2019 03:24 PM
Subject: Next Steps for Steering Committee on Modernization of Price Review Process Guidelines

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Dear Steering Committee Members,

In preparation for our last meeting please find attached a word document which contains all the questions that have been posed for the SC as part of the consultation process.

We introduced the proposed questions at our first face-to-face meeting June 25th ,

along with the proposed new PMPRB Guidelines Framework. Subsequent meetings focused on identifying possible topics for the Technical Working Group (TWG) as well as unpacking each aspect of the proposed framework and soliciting feedback. At our meeting in December, hypothetical case studies were presented in order to demonstrate how the framework could work in practice and provided an assessment of current guidelines relative to the proposed ones. Most recently, the SC received a copy of the Final Technical Working Group Report and the chair, Dr. M. Paulden, provided a webcast on the recommendations. We would like to offer the SC an additional opportunity to ask any follow up or clarifying questions on the TWG report. As has been the practice with feedback, please ensure to pose the questions with a cc to the entire SC before **March 29th**. Attached for your benefit is a copy of the presentation from the webcast.

We kindly ask you to provide your final formal feedback to the specific questions that had been identified by Board Staff on the attached questionnaire. Your responses along with other feedback that has already been received will be reflected in the final Steering Committee Draft report which we will circulate in advance of our next meeting. Steering Committee members will be provided with an opportunity to review the draft and ensure that we have accurately captured your feedback in the report. SC members will also be given an opportunity to speak to their feedback at the meeting to ensure everyone can hear the perspective directly.

We ask that you fill out the questionnaire by **April 8th.** We will be following up shortly with a doodle poll to see what dates work best for SC members in early May.

Sincerely,

**Tanya Potashnik**
Director, Policy and Economics Analysis Branch | Direction des politques et de l'analyse économique
Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés
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Government of Canada | Gouvernement du Canada

[attachment "Recommendations of the Technical WG.pptx" deleted by Stephen Frank/Toronto/CLHIA] [attachment "Steering Committee Questionnaire_final.docx" deleted by Stephen Frank/Toronto/CLHIA]

Patented Medicine Prices Review Board (PMPRB)

# Questionnaire for the Steering Committee on Modernization of Price Review Process Guidelines

Due date for receiving responses: **COB April 8th, 2019**

## Topic 1: Use of external price referencing (EPR): median international price test (MIPC)

- The proposed approach is that all new medicines are assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).
- The MIPC would be recalculated annually until there are at leasdfast 7 countries or 3 years post first date of sale. At that point the MLP would no longer be interim. This approach provides both predictability (e.g., exchange rate fluctuations) and reduces regulatory burden.
- Re-benching could result in the MLP being adjusted over time.
- IMS will be used to verify international list prices however filing requirements for patentees will remain unchanged for the new schedule.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

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| Stakeholder input/comments: Based on the proposed new basket of 12 countries, this appears to be a reasonable change. Excluding the US from the 12 countries, does respond to the joint recommendation through the pCPA. |

2. **Should exceptions be made to the MLP-MIPC test and, if so, when and why?**

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| Stakeholder input/comments: There could be consideration if under exceptional circumstances there is a significant situation where prices reported do not reflect the current market conditions – evidence must be presented through a centralized process and adjudicated. |

3. **Should there be a price floor for Category 2 medicines based on Lowest International Price Comparison (LIPC)?**

| Stakeholder input/comments: A price floor for Category 2 medicines may discourage market competition. This would not be in the interest of payers. |
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4. **Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?**

| Stakeholder input/comments: Yes, this is a reasonable approach. |
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5. **Should an increasing gap between MIPC and the MLP trigger a re- bench?**

| Stakeholder input/comments:Yes. |
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6. **Should EPR differ depending on category or vintage of the patented medicine?**

| Stakeholder input/comments: The EPR could be adjusted to accommodate significant price differentials with respect to vintage patented medicine to mitigate shock to the market. |
|---|

## Topic 2: Use of List and Net Price Ceilings

- The conceptual framework presented to the SC at the first meeting proposed the establishment of two ceilings for Category 1 medicines based on both list (MLP) and net (rebated) prices (MRP).
- For Category 2 medicines, the proposal is to establish one ceiling (MLP) based on list prices domestically and internationally based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC). No Category 2 medicine will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- The approach aims to establish a net price ceiling to both protect Canada's true transaction price from being exposed and allow patentees to comply with the net price ceilings through use of all discounts/rebates direct and indirect.

## Questions

1. **Should a Category 1 medicine ever have more than one MRP?**

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| Stakeholder input/comments:No, it is administratively difficult to maintain/implement different price points across PTs/payers. The lowest price for all PTs should be used if possible. |

2. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

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| Stakeholder input/comments:There could be consideration if under exceptional circumstances there is a significant situation where prices reported do not reflect the current market conditions – evidence must be presented through centrailized process and adjudicated. |

3. **Should confidential third party pricing information only be used for compliance purposes?**

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| Stakeholder input/comments:In principle, if confidential pricing information is available, it should be applied to all pricing assessments. |

## Topic 3: Risk Assessment and Prioritization Criteria for Category 1 & 2 medicines

- The second part of the framework consists of a screening phase which would classify new patented medicines as either high or low priority based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans).
- The framework proposed high level criteria that PMPRB would use to categorize medicines as Category 1 or 2:
    - First in class or substantial improvement over existing medicines for clinically significant indication(s)

  - Market Size >Affordability Threshold
  - ICER > maximum opportunity cost threshold
  - Annual or treatment cost> per capita GDP
- Medicines that appear to be high priority based on these screening factors would be subject to automatic investigation and a comprehensive review to determine whether their price is potentially excessive.

## Questions

1. **Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?**

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| Stakeholder input/comments:This appears to be a reasonable regulatory approach. Further considerations can be made once impact is evaluated. |

2. **Should further categories exist with different treatment modalities?**

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| Stakeholder input/comments:Yes, based on an on-going assessment of the market conditions/dynamics, other categories/modalities should be considered to achieve best value. |

3. **Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?**

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| Stakeholder input/comments:Recognzing the rapid pace of changing technology, based on the market conditions/dynamics, criteria should be continuously maintained and updated. Setting the threshold should be based on standard practice/evidence set and maintained by the knowledge experts. |

4. **Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?**

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| Stakeholder input/comments: PE and market size factors should apply both as screens and thresholds. Fundamentally, should be pricing based on the effectiveness and utility of the drug. A GDP factor is unnecessary. |

5. **Should Category 2 medicines be scrutinized more or less than proposed?**

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| Stakeholder input/comments:Yes, similar to other jurisdictions, medicines that have been on the market for a long period of time should be subject to an on-going price review (market testing) and/or subject to a regulated price decrease (i.e. 5% regulated price decrease after the medicine has been on the market for a long time – 3 to 5 years unless the change causes financial harm/impacts business viability or not being able to supply medicines to the market. |

## Topic 4: Re-Benching Criteria

- All new medicines will be given an interim MLP of 3 years or until the medicine is sold in 7 countries, whichever comes first.
- MLP is then frozen, as is MRP, unless re-benching is triggered by one of the following criteria:
    - Approval of a new indication
    - Sales in excess of expected market size
    - New evidence on cost-effectiveness (e.g. CADTH therapeutic class review or lifting of HC conditions on NOC)
    - Significant changes in international prices (eg. MIPC < MIPC at intro by more than 25%)
- Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI
- Complaints received by the PMPRB will trigger an investigation, during which the PMPRB will assess whether:
    - The medicine is in compliance with the Guidelines; and
    - Whether circumstances in the market have changed to warrant a re-benching/reclassification.

### Question

1. **How often and in what circumstances should a medicine be re-benched?**

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| Stakeholder input/comments: Criteria as set out. |

## Topic 5: Tests for Category 1 Medicines

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).
- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

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| Stakeholder input/comments: Yes, assuming the 12 countries are reflective of the global market. On-going market sounding should be applied to ensure best market value. |

2. **Should exceptions be made to the MIPC test and, if so, when and why?**

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| Stakeholder input/comments: Based on the rapid pace of changing technology , there should be consideration for exceptions only if under exceptional circumstances. It must represent a significant situation where prices reported do not reflect the current market – evidence must be presented by a standardized process and adjudicated. |

3. **Should the cost effectiveness threshold for Category 1 drugs vary?**

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|---|
| Stakeholder input/comments: No, the most cost effective amount should be applied consistently for the category. Exceptional cases can be re-assessed (as required). |

4. **Should a Category 1 medicine ever have more than one MRP?**

| Stakeholder input/comments: No, too difficult to manage/administer different prices across PTs. Our goal is to establish a best price for all PTs. |
|---|

5. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

| Stakeholder input/comments: Consideration for only exceptional situations – evidence must be provided and validated by a standardized process. |
|---|

## Topic 6: Tests for Category 2 Medicines

- Category 2 medicines have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex- factory) prices, domestically and internationally.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?**

| Stakeholder input/comments: The approach described above appears reasonable. |
|---|

2. **Should exceptions be made to the MIPC test and, if so, when and why?**

| Stakeholder input/comments: No. |
|---|

3. **Should there be a price floor for Category 2 drugs and, if so, should it be based on LIPC?**

| |
|---|
| Stakeholder input/comments: No floor price is preferred however the LIPC approach suggested is reasonable. |

4. **Should Category 2 drugs be scrutinized more or less than proposed?**

| |
|---|
| Stakeholder input/comments: Category 2 drugs should be scrutinized regularly. Medicines on the formulary over 5 years should be considered for statutory price reductions as occurs in other jurisdictions. |

## Topic 7: Use of Confidential Pricing Information

- Price reviews would be conducted for the following customer classes:
  - National/Provincial Retail – list price assessed against MLP
  - National Private Payer – ATP assessed against MRP
  - Provincial Public Payer – ATP assessed against MRP in each market
- ATPs are calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

### Questions

1. **Are the proposed definitions of markets and customer classes reasonable?**

| |
|---|
| Stakeholder input/comments: Yes, if confidential pricing information is available. |

2. **Is the proposal to use third-party pricing information for compliance with the MRP reasonable?**

| |
|---|
| Stakeholder input/comments: Yes, if confidential pricing information is available. |

## Topic 8: Application of New Regime to Existing Medicines

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 drugs would be re-benched later unless a complaint is received.
- All drugs within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to come into compliance.

### Questions

1. **Is the use of MIPC as an interim ceiling reasonable?**

| Stakeholder input/comments: Yes. . |
|---|

2. **Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?**

| Stakeholder input/comments: Yes although there could be some consideration of a transition period to allow for business adjustments. |
|---|

3. **Are there reasonable alternative approaches to bringing existing medicines under the new framework?**

| Stakeholder input/comments: see above |
|---|

## General Question

**Are there any other questions or comments that you would like to share with the SC that have not been captured above?**

Stakeholder input/comments: BC fully supports the modernization efforts and appreciates all the work that has been accomplished as an important step towards ensuring drug prices are not excessive and the sustainability of public drug plans.

| | |
|---|---|
| **From:** | Iman Mohamed |
| **To:** | Tanya Potashnik; Matthew Kellison |
| **Cc:** | laurene.redding@astrazeneca.com; Paul Petrelli |
| **Subject:** | Final Steering Committee meeting May 13, 2019 |
| **Date:** | Friday, May 10, 2019 5:10:40 PM |
| **Attachments:** | BIOTECanada Case Studies May 13, 2019.pdf |

**Sent on Behalf of the BIOTECanada Steering Committee members Laurene Redding and Paul Petrelli:**

Dear Tanya,

Thank you for sharing the agenda and the draft report.

It would be helpful if at the start of the meeting you and Matthew could provide Steering Committee members with some clarity regarding the following:

1. What is the objective PMPRB wants to get at the end of the meeting? Are there decisions points PMPRB staff would like to see addressed at the meeting related to the report and discussion?
2. Where do you anticipate recommendations for draft guidelines be discussed on the agenda?
3. Will there be an opportunity to receive responses from PMPRB on the questions and comments raised by members throughout the Steering Committee process?

As discussed at the Dec. 13, 2018 SC meeting, BIOTECanada would also like to take some time to share with the Steering Committee revised case studies attached.

Thank you
Laurene & Paul

Iman Mohamed
Director, Health Policy
BIOTECanada
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# BIOTECanada Case Studies

## Final Steering Committee Meeting

## May 13, 2019

# Summary of Cases

| | Treatment cost (annual or full regimen) | Potential treatment population (annual) | Potential annual revenues | Profile | Potential disease area |
|---|---|---|---|---|---|
| Case 1 | $294 per capsule | 1400 | $150M | Treats a chronic condition<br>One approved indication<br>Has no comparators<br>Small treatment population | Oncology |
| Case 2<br>Total market under current regulations | $300K | 250 diagnosed | $75M | • Rare disease drug with one indication<br>• Significant clinical improvement Health Canada<br>• No approved comparators<br>• Small treatment population, high severity of illness, unmet need | DRD |
| Case 2<br>New regulations | $108K | 100 Medically eligible for treatment** | $10.8M | | |
| Case 3 | $32,600 | 85,000 to 100,000 | $3,2B | Multiple indications<br>Autoimmune therapy<br>Second indication for separate for of disease | Autoimmune |

# Acronyms

HIPC – Highest international price comparison

MIPC –Median international price comparison

LIPC – Lowest international price comparison

TCC – Therapeutic class comparison

MLP – Maximum list price

MAPP – Maximum average potential price

MRP – Maximum rebated price

NEAP – Non-excessive average price

HTA – Health Technology Assessment

QALY – Quality-adjusted life year gained

ICER – Incremental cost-effectiveness ratio

PV – pharmacoeconomic value

$/QALY – cost per quality adjusted life years gained

RWE – Real world evidence

# BIOTECanada Case 1 – Small Molecule Capsule Product for Metastatic Cancer

- Treats a chronic condition
- Has no therapeutic comparators
- One approved indication by Health Canada (HC)
- small treatment population
  - Possible indications: oncology
- Annual treatment cost (list price): $294 per capsule
- Population with the condition: 1,400
- Potential annual revenues based on the total treatment population: $150M
- Category 1 due to ICER threshold, market size

# Case 1 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $352 | $394 | $262 | $275 | $275 | $275 | $275 |
| PV Threshold Price** | N/A | $95 | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $30M | $30M | $30M | $30M | $30M | $30M |
| Market Size Adjustment *** | N/A | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV |
| MRP | N/A | $191 | $191 | $191 | $191 | $191 | $191 |
| Total revenue at MRP | N/A | $60M | $60M | $60M | $60M | $60M | $60M |

*MLP/MRP frozen.
**PV threshold used is $60,000/QALY. Manufacturer's model was used for calculations. Highest ICER selected for 'primary indication' using current PMPRB selection rules.
***Population size is ~1400 people. Rare disease market adjustment used.
Revenue values are for illustrative purposes only.

# Case 1 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$294** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $317 (interim price)<br>$345 (final price) | Ex-factory price ceiling (MLP): $275<br><br>Rebated price ceiling (MRP): (frozen at year 3): $191 |
| Tests used to set the Ceiling | MIPC (moderative improvement with no comparators) | MLP: MIPC<br>MRP: 2 * PV price |
| Ceiling percent reduction from original price | none | MLP: 7%<br>MRP: 35% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 2 – Rare disease drug

- Rare disease drug with one indication
- Clinically significant improvement
- High burden of illness and high unmet need
- No therapeutic alternative
- 250 Canadians diagnosed w/condition (~100 patients meet criteria for treatment)
- Annual treatment cost: $300,000
- High priority for Health Canada and CADTH
- Under new regulations, potential annual revenues based on the total treatment population: $10.8M peak sales (~100 patients)
- Category 1 based on no therapeutic alternative and annual treatment cost above GDP/capita

# Case 2
# Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC)* | $300K | $300K | $300K | $300K | $300K | $300K | $300K |
| PV Threshold Price** | N/A | $54K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price*** | N/A | $1.1M | $2.2M | $3.3M | $4.4M | $5.4M | $5.4M |
| Market Size Adjustment**** | N/A | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV |
| MRP | N/A | $108K | $108K | $108K | $108K | $108K | $108K |
| Total revenue at MRP | N/A | $2.2M | $4.4M | $6.6M | $8.8M | $10.8M | $10.8M |

*MLP/MRP frozen.
**Assume 82% price reduction required to meet PMPRB PV threshold of $60K/QALY, based on CADTH PE Report
***20% share growth per year. 100% of share in year 4 & 5
***Positive market size adjustment owing to rare disease small market size – 2xPV Threshold price.

# Case 2
# Current vs New Proposed Guidelines

| | *Current Guidelines* | *Proposed Guidelines* |
|---|---|---|
| **Price Ceiling** | $300K at launch<br><br>Within guidelines | Ex-factory price ceiling (MLP): $300K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $108K |
| **Tests used to set the Ceiling** | Midpoint of top of TCC and MIPC (moderate improvement, no comparators) | MLP: MIPC<br>MRP: 2xPV price |
| **Ceiling percent reduction from original price** | 0% ($300K launch price is at MIPC) | MLP: 0% (300K)<br>MRP: 64% (from 300K to 108K) |
| **Compliance assessment made against** | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

**Provincial Confidential discounts not included in calculation

# Case 3 – Autoimmune Therapy, multiple Indications

- Indication at launch for adults with autoimmune disease
- Treats 2 chronic condition
  - Condition 1 has multiple available treatments – S/N Improvement
  - Condition 2 has no comparators (i.e., first treatment for condition)
- Total estimated 85,000 to 100,000 patient population
- Comparator 2 patient population: < 5 in 10,000 (i.e., < 18,000)
- Annual treatment cost (list price): $32K
- Potential annual revenues based on the total treatment population: $3.2B
- Category 1 based on ICER, market size

# Case 3 – Application of the Proposed Guidelines (first indication)

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $8.6K | $8.6K | $8.5K | $8.5K | $8.5K | $8.5K | $8.5K |
| PV Threshold Price *** | N/A | $5.7K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $137M | $201M | $237M | $348M | $426M | $507M |
| Market Size Adjustment | N/A | 50% | 50% | 50% | N/A | N/A | N/A |
| MRP | N/A | $4,102 | $3,704 | $3,575 | $3,575 | $3,575 | $3,575 |
| Revenue at MRP | N/A | $99M | $131M | $149M | $204M | $243M | $284M |

**MRP frozen after 3 years.
*** ICER threshold used is $60K/QALY.
Revenue values used for illustrative purposes only.

# Case 3 – Application of the Proposed Guidelines (second indication)

No comparators

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MIPC | $8.6K | $8.5K | $8.5K | $8.5K | $8.5K | $8.5K | $8.5K |
| PV Threshold Price | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| MLP=higher of LIPC and median TCC | $8.6K | $7.6K | $7.6K | $7.6K | $7.6K | $7.6K | $7.6K |
| Revenue at MLP | $99M | $143M | $195M | $249M | $304M | $362M | $?M |
| Market Size Adjustment | N/A (i.e., 2xPV) | N/A (i.e., 2xPV) | N/A (i.e., 2xPV) | N/A (i.e., 2xPV) | N/A (i.e., 2xPV) | N/A (i.e., 2xPV) | N/A (i.e., 2xPV) |
| MRP | $4,102 | $3,704 | $3,575 | $3,575 | $3,575 | $3,575 | $3,575 |
| Revenue at MRP | $99M | $143M | $195M | $249M | $304M | $362M | $?M |

**MRP frozen after 3 years.
Revenue values used for illustrative purposes only.

# Case 3 –Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$8600** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling Indication 1 | $80K | Ex-factory price ceiling (MLP): $8.5K<br><br>Rebated price ceiling (MRP): $4.1K |
| Price Ceiling Indication 2 | $80K | Ex-factory price ceiling (MLP): $7.6K<br><br>Rebated Price ceiling (MRP): $4.1K |
| Tests used to set the Ceiling | TCC | MLP: MIPC for condition 1<br>LIPC for condition 2<br>MRP: based on PV and Market Size Adjustment for condition 1 |
| Ceiling percent reduction from original price | None | MLP: 1%, 12%<br>MRP: 52%; 52% |
| Compliance assessment made against | ATP (rebated price, rebates include free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

| | |
|---|---|
| **From:** | Declan Hamill |
| **To:** | Tanya Potashnik; Claudia Lacroix; Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; Stephen Frank; jim@canadiangenerics.ca; kvoin@clhia.ca; jody@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; Pamela Fralick; durhane@optimizinghealth.org; durhane@sympatico.ca; Blackmer, Jeff; Adams, Owen; Glen Doucet; Joelle Walker; gail@badgut.org; melias@myeloma.ca; Doidge, Scott: HC; susan.pierce@canada.ca; patrick.dufort; Brittany.Nagy@ontario.ca; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow; annie.gariepy@inesss.qc.ca; julie.aubin@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; Gesine Freund; Christina@canadiangenerics.ca; Marie-Anne Paquette; Pascale Clement; Clark, Karen; megan.steen@canada.ca; Riedstra, Erynne (MOHLTC); ryan.redecopp@canada.ca; Guillaume Couillard; Theresa Morrison; Elena Lungu; Richard Lemay; Linda Payant; Isabelle Demers; Murielle Marie; Matthew Kellison; Isabel Jaen Raasch |
| **Subject:** | RE: Materials for May 13th Meeting of PMPRB SC - Email 1 of 2 |
| **Date:** | May 17, 2019 11:46:51 AM |

Dear Tanya:

Further to the May 13th meeting, thank you for providing IMC with a final opportunity to comment on the draft Steering Committee (SC) report.

1. From an organization perspective, we agree with other SC members who noted during the May 13th meeting that the stakeholder feedback received should be more prominently featured for the PMPRB's Board in the final report, rather than being placed in appendices at the end of the document.
2. IMC is concerned about the classification of some SC feedback as being within (Appendix 8.4/ "Appendix") and outside (Appendix 9/ "Annex") the scope of the SC Terms of Reference. IMC views this as a subjective artificial differentiation and, more importantly, one that could be used to potentially dismiss or devalue feedback deemed to be "outside the scope". IMC also respectfully disagrees that its feedback was not within scope. For example, IMC's email dated July 13, 2018 contained specific questions relevant to issues related to the proposed PMPRB framework. To avoid any subjectivity regarding the categorization of the SC comments received, IMC requests that all SC feedback received by the PMPRB be consolidated in one appendix (or other organizational unit, if the structure of the final report is different from the draft report). Page 12 of the report should also be amended to reflect that IMC did provide written feedback.
3. IMC acknowledges that PMPRB staff advised SC members on May 13th that they would be providing the PMPRB Board with comments and/or analysis on the SC feedback received, and that this would not be shared with the SC members. For transparency and given the significant time allocated by SC members to the committee process since June 2018, IMC believes that any PMPRB staff comments and/or analysis on the feedback received should be shared by PMPRB staff with SC members before it is provided with the final SC report to the PMPRB Board, and with a reasonable opportunity for SC members to respond or comment. SC members should not have to submit Access to Information requests to obtain such comments and/or analysis.

Please contact me if you have any questions.

Sincerely,

Declan Hamill
**DECLAN HAMILL**

*Vice President, Legal, Regulatory Affairs & Compliance*
*Vice-président, Affaires juridiques et réglementaires,et Conformité*

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**From:** Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>
**Sent:** Tuesday, May 7, 2019 3:19 PM
**To:** Claudia Lacroix <claudia.lacroix@pmprb-cepmb.gc.ca>; Tanya Potashnik <tanya.potashnik@pmprb-cepmb.gc.ca>; Suzanne.Mcgurn@ontario.ca; Imran.S.Ali@ontario.ca; Mitch.Moneo@gov.bc.ca; michael.sherar@cancercare.on.ca; robin.mcleod@cancercare.on.ca; BrianO@cadth.ca; luc.boileau@inesss.qc.ca; sylvie.bouchard@inesss.qc.ca; Karen.reynolds@canada.ca; eric.dagenais@canada.ca; rodrigo.arancibia@canada.ca; Stephen Frank <sfrank@clhia.ca>; jim@canadiangenerics.ca; kvoin@clhia.ca; jody@canadiangenerics.ca; laurene.redding@astrazeneca.com; Paul.Petrelli@jazzpharma.com; Pamela Fralick <pfralick@imc-mnc.ca>; Declan Hamill <dhamill@imc-mnc.ca>; durhane@optimizinghealth.org; durhane@sympatico.ca; Blackmer, Jeff <Jeff.Blackmer@cma.ca>; Adams, Owen <owen.adams@cma.ca>; Glen Doucet <gdoucet@pharmacists.ca>; Joelle Walker <jwalker@pharmacists.ca>; gail@badgut.org; melias@myeloma.ca; Doidge, Scott: HC <scott.doidge@hc-sc.gc.ca>; susan.pierce@canada.ca; patrick.dufort <patrick.dufort@inesss.qc.ca>; Brittany.Nagy@ontario.ca; Charlotte.elagab@gov.bc.ca; Rajni.Vaidyaraj@cancercare.on.ca; adriana.ruiz@cancercare.on.ca; chantale.beauchamp2@canada.ca; Roxanne Blow <RoxanneB@cadth.ca>; annie.gariepy@inesss.qc.ca; julie.aubin@inesss.qc.ca; celine.makischuk@canada.ca; amanda.janes@canada.ca; adsa@clhia.ca; Gesine Freund <gfreund@imc-mnc.ca>; Christina@canadiangenerics.ca; Marie-Anne Paquette <mapaquette@imc-mnc.ca>; Pascale Clement <pclement@imc-mnc.ca>; Clark, Karen <Karen.Clark@cma.ca>; megan.steen@canada.ca; Riedstra, Erynne (MOHLTC) <Erynne.Riedstra@ontario.ca>; ryan.redecopp@canada.ca; Guillaume Couillard <guillaume.couillard@pmprb-cepmb.gc.ca>; Theresa Morrison <Theresa.Morrison@pmprb-cepmb.gc.ca>; Elena Lungu <elena.lungu@pmprb-cepmb.gc.ca>; Richard Lemay <richard.lemay@pmprb-cepmb.gc.ca>; Linda Payant <linda.payant@pmprb-cepmb.gc.ca>; Isabelle Demers <isabelle.demers@pmprb-cepmb.gc.ca>; Murielle Marie <murielle.marie@pmprb-cepmb.gc.ca>; Matthew Kellison <matthew.kellison@pmprb-cepmb.gc.ca>; Isabel Jaen Raasch <isabel.jaenraasch@pmprb-cepmb.gc.ca>
**Subject:** Materials for May 13th Meeting of PMPRB SC - Email 1 of 2

Dear Steering Committee Members,
Please find attached materials (translation pending) for our upcoming meeting in Ottawa. Appendix will be sent in a separate email due to size restrictions. You will also be able to locate the materials on Brightshare. For those of you unable to join us in person, we have added dial in information to the meeting invite.

We welcome your comments on the draft agenda. You'll note that in response to the feedback received to date on the Technical Working Group Report and Recommendations, we have invited the chair to present to the SC in person. We trust this will be helpful for the SC members to gain a better understanding of the recommendations and their relevance. The afternoon is dedicated to discussing feedback received as well as reviewing the final SC report. We would like to invite members of the SC to speak to their feedback directly. Should anyone wish to do so, please let me know in advance so we can allocate the time on the agenda accordingly.

We look forward to the upcoming meeting.

Sincerely,

*Tanya*

Tanya Potashnik
Director, Policy and Economics Analysis Branch | Direction des politques et de l'analyse économique
Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés
Box L40, 333 Laurier Avenue West, Suite 1400 | Boîte L40, 333, rue Laurier ouest, Bureau 1400
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BIOTECanada

May 27, 2019

Dr. Mitchell Levine
Chairman
Patented Medicine Prices Review Board
Box L40, 333 Laurier Ave. West, Suite 1400
Ottawa, ON K1P 1C1

Dear Dr. Levine,

On behalf of the members of BIOTECanada, I am writing to you in your role as a Chair of the PMPRB to express the industry's concerns regarding the PMPRB modernization initiative's Steering Committee (SC) process which has recently concluded. The industry draws these process and content concerns to your attention at this time as they are important considerations given the PMPRB is rapidly moving ahead with the development of draft guidelines to implement the proposed changes to the regulatory regime overseeing prices and access to new medicines and therapies in Canada.

The industry appreciates the government's initiative and commitment to ensuring timely and affordable access to medicines for all Canadians. Indeed, BIOTECanada welcomed the opportunity to contribute to the SC work as it represented an important process through which the industry could constructively provide its input and experience in other jurisdictions towards the regulatory development process. However, despite a consultation which was intended to inform the development of guideline reforms, with the final SC meeting last week it is clear that the process led to few constructive recommendations or meaningful amendments to the proposed guideline framework. Correspondingly, the industry remains concerned that the regulatory package and accompanying guidelines will significantly impact the ability of Canadian patients to have timely access to therapies and medicines.

Specifically, several key issues impact the integrity and credibility of the SC consultation, namely:

1. The SC diverted from its original mandate to assist the PMPRB to synthesize stakeholder views on key technical and operational modalities of new draft guidelines that would give effect to the proposed amendments to the patented medicines regulations. As a result, the SC made no recommendations and provided no guidance to improve the implementation of the proposed regulatory package;
2. The input of various SC members (not only industry) was frequently called into question by the SC Co-Chairs throughout the process; and,
3. The SC failed to address many important technical and operational uncertainties impacting the implementation of the proposed reforms.

All told, it is unclear how the SC process has contributed in any meaningful way to improve the regulatory framework or inform the development of the corresponding guidelines.

The SC process significantly diverted from the expectations set out in the Terms of Reference. The mandate of the SC was to assist the PMPRB as it sought to:

1. Operationalize Health Canada's proposed amendments to the Patented Medicines Regulations to make drugs more affordable for Canadians; and,
2. Enable the PMPRB to make more efficient use of its resources through a risk-based approach to drug price regulation that simplifies and streamlines compliance for patentees.

Having reached the end of the SC process, neither of these key objectives have been met.

The SC Terms of Reference state "a report of the SC deliberations, and any associated advice or recommendations, will be prepared by the PMPRB staff". At the conclusion of the SC process, PMPRB staff did not provide a set of recommendations for SC review and only confirmed at the May 13 final

submit to the Board. Indeed, given the "final report" is being presented to the Board as is, SC members are questioning how any of the SC input will be included in the report and its recommendations.

The disregard for the SC process is further demonstrated in the draft final report which failed to capture the deliberations of the SC. Moreover, it presents only a high-level summary of elements unilaterally determined important by the PMPRB staff, while omitting any engagement with the concerns raised by SC members. The feedback provided by SC members was dismissed by the Co-Chairs as being either out of scope or too detailed for this stage of the consultation process. This clearly fails to adhere to the SC's Terms of Reference which state, "the Co-Chairs will make every effort to ensure the SC's final report accurately reflects any important points of convergence or contention between members".

Ultimately, it is clear the SC was established as a table for PMPRB staff to inform stakeholders, not solicit input to improve the development guidelines. Meetings were often one-way briefing sessions, with PMPRB presenting a framework but not seeking input from SC members. Amendments made to the framework were relegated to the footnotes of the draft report and those amendments were not discussed at the SC, but rather presented as a fait accompli. Importantly, the framework itself includes many pieces that have been left as placeholders rather than clear and defined elements for further discussion.

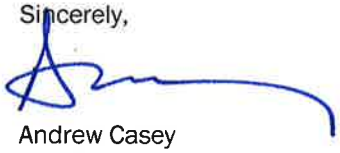
To date, many questions and discussion points raised at SC meetings remain unaddressed. The industry raised a number of questions during the SC consultation process regarding how the proposals will be implemented and operationalized. Importantly, the operational requirements and the numerous practical and commercial challenges to implementing what is being proposed was provided only cursory attention. Indeed, many times, throughout the process SC members were told operational concerns raised were contrived and should not be a barrier to what PMPRB is proposing.

Without addressing several of the practical challenges identified by SC members, Canada will be out of step with other similar jurisdictions. Correspondingly, the multinational companies operating in Canada will be forced to revisit the tenability of continued exposure and services to the Canadian health system. This will negatively impact industry investment in Canada and will lead to a delay in access to new therapies for Canadian patients.

It is important to reiterate the industry is very aware of the fiscal pressures governments are under in relation to healthcare and supports the need to develop solutions to mitigate healthcare costs, of which medicines and therapies are one part. Correspondingly, the industry viewed the SC as an important and meaningful opportunity to develop an effective and functioning regulatory framework. In this context, the lack of clear outcomes emerging from the SC process and the dismissal of SC member perspectives in the final report, raises deep concerns regarding the report's objectivity and substance.

A comprehensive and effective policy approach to pricing is needed to ensure: the sustainability of the healthcare system; the continued access to advanced therapies for patients; and, a robust environment for the development and commercialization of Canadian innovation. In this context, the industry urges you to consider these objectives as the PMPRB Board reviews the draft SC deliberations and report that will inform the development of draft guidelines that will guide the implementation of proposed regulatory reforms.

Sincerely,



Andrew Casey
President and CEO

cc: Douglas Clark, Executive Director PMPRB
Steering Committee members

INNOVATIVE MEDICINES CANADA | MÉDICAMENTS NOVATEURS CANADA

*President's Office | Bureau du Président*

May 27, 2019

Dr. Mitchell Levine
Chairperson
Patented Medicine Prices Review Board
Box L40, 333 Laurier Avenue West, Suite 1400
Ottawa, ON K1P 1C1

Dear Dr. Levine:

**Re: IMC Comments on the PMPRB Steering Committee and Technical Working Group Processes**

On behalf of the members of Innovative Medicines Canada (IMC), I am writing to express some of the major concerns of the innovative pharmaceutical industry regarding the Patented Medicine Prices Review Board (PMPRB)'s Steering Committee (SC) and Technical Working Group (TWG) processes. As noted at the start of the SC and TWG processes, IMC opposes the proposed regulatory changes set out in Canada Gazette Part I (December 2017). The following comments do not concern the substantive nature of these regulatory proposals, but rather the significant shortcomings of the SC and TWG processes.

Despite the significant time and resources allocated by PMPRB and stakeholder representatives over nearly one year, the processes have demonstrated that the new regime will not function efficiently and effectively in the event that the proposed changes to the *Patented Medicines Regulations* are finalized as currently proposed:

- A key outcome from the TWG process was the lack of technical consensus on the proposed new economic factors; and
- A key outcome from the SC process was additional uncertainty for patentees and other stakeholders with respect to how the changes would be applied in practice.

While many of our process concerns are already on the record, IMC wishes to emphasize several key issues that emerged during the SC and TWG now that both have concluded their work, and the SC report is to be finalized by PMPRB staff and presented to the PMPRB Board shortly.

**No consideration of feasibility concerns**

Throughout the TWG process, PMPRB representatives consistently prevented discussion of critical feasibility and implementation issues. This was unfortunate given the TWG was specifically charged with consideration of technical questions related to implementation. The feasibility issues that industry members attempted to raise were substantive enough that patentees subject to the proposed regulation changes cannot currently comply with the new regime. Based on the SC and TWG discussions, we do not believe that

the proposed regulatory changes can be implemented as envisioned and respectfully disagree with statements by PMPRB representatives that the "details" can be addressed at a later date.[1]

**No TWG agreement on new economic factors and imposed public healthcare system perspective**

Despite some agreement on the high-level recommendations, no consensus was reached at the TWG regarding the implementation of the proposed new economic factors (pharmacoeconomic value, market size, and GDP/per capita) for the purpose of setting price ceilings for patented medicines in Canada. The TWG did not resolve the issue of how thresholds could be determined.[2] The industry representatives and other TWG members identified issues related to uncertainty and lack of clarity, as well as the significant technical and operational issues associated with the application of the proposed economic factors. The TWG observations and recommendations also made plain the evidentiary gaps and uncertainty that exists around the proposed pharmacoeconomic value factor.[3]

In addition, throughout the process, TWG members were required by PMPRB staff to adopt a "public health care system perspective" when the question of the appropriate perspective was assigned to the TWG for deliberation and recommendation. This significant limitation in scope does not reflect the mixed public/private market Canadian environment and unreasonably restricted the TWG's deliberations.[4] As a result, many of the TWG's recommendations are open-ended and frequently defer to the PMPRB's "policy intent."

**Reporting of confidential information remains highly problematic**

The SC and TWG processes provided no information regarding how the proposed disclosure of payment information could be incorporated into a new price regulation framework. Moreover, it is not possible for patentees – who do not sell to payors – to report according to a national public and national private market price. For this and other reasons, it is unclear whether patentees will be able to comply with the new regime. IMC also questions the feasibility of protecting this commercially sensitive and confidential information if it is to be used for the purposes of price ceiling regulation.

**PMPRB case studies inconsistent with Health Canada regulatory impact assessment**

From the outset of the SC process in mid-2018, industry and other stakeholders requested product case studies from PMPRB to provide some clarity on the practical impact of the proposed new regime. In

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[1] For example, there were no discussions on feasibility and jurisdictional issues regarding the use of confidential information, including but not limited to, the significant time that can elapse between market entry and conclusion of a third-party agreement (IMC email, July 13, 2018).

[2] TWG representatives presenting their report to the SC on May 13, 2019 indicated that it could take as much as 2 ½-3 years to obtain the data required to properly inform these measures.

[3] For example, "The Working Group was unanimous in considering the empirical evidence base with respect to Canadian estimates of supply-side thresholds to be uncertain" (TWG Report, p.23).

[4] The two systems currently in place are very different, with different sources of funding, different purposes and different constituents/recipients.

response, PMPRB representatives presented case studies to the SC in December 2018, and to the TWG in February 2019.

The magnitude of the price reductions illustrated by some of the PMPRB case studies was substantially greater than the impacts suggested by Health Canada's Regulatory Impact Analysis Statement and the Cost-Benefit Analysis that were released with the draft regulatory amendments in December 2017.[5] When this issue was raised at the TWG, it was not adequately addressed by PMPRB staff.[6] Similarly, and despite stakeholder questions placed on the record during the SC process, no clarity on this issue was provided.

**Out of sequence presentation of case studies**

In the PMPRB staff's view, the product case studies were not relevant to the work of the TWG. Indeed, the case studies were only made available at the end of the TWG deliberations, and a review and discussion of the six case studies was limited to thirty-five minutes on the agenda of the final TWG meeting. Notwithstanding the opposition of the industry to many of the proposed regulatory changes, the objective of the SC and TWG processes should have been to work in coordination to yield a better collective understanding of how the new system would work in practice. It is concerning that the expert group specifically created and selected by the PMPRB to address technical implementation issues was not afforded a meaningful opportunity to consider the case studies.[7]

**No discussion of Category Two products**

PMPRB staff focused the discussions during the SC and TWG almost exclusively on the proposed Category One products. While the screening criteria for the two categories has not yet been firmly established, PMPRB has advised that Category Two products may comprise the bulk of the products under the proposed new system. Our industry continues to have serious concerns about any potential move to an "average" therapeutic class comparison. If Category Two would indeed include the majority of products as stated by PMPRB, then far more discussion and consultation is required on the regulation of these products before any Guideline changes are implemented. It is also worth noting that Category Two products have comparators and, in many instances, have generic competitors. Any policy change in this area seems to contradict PMPRB's stated desire to focus its regulatory effort on products where there is a higher risk of abuse of monopoly power.[8]

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[5] These case studies focused solely on Category 1 medicines and introduced factors (e.g., the Lowest International Price Comparison (LIPC) test) that had not previously been introduced. They also did not reflect the reality of the marketplace in terms of complexity, for example, with oncology medicines that have multiple indications over the patent life of the product.
[6] See TWG report, p. 185.
[7] A better process would have been for the PMPRB to first present the case studies to the TWG for their expert analysis and, following any changes, for PMPRB to present the reviewed and improved case studies to the SC. Instead, the case studies were presented to the SC, consisting almost entirely of non-experts, in some detail.
[8] Considering the additional regulatory burden created by proposed PMPRB reforms, IMC also questions if they are aligned with the Government's new Regulatory Roadmaps and Directive on Regulations calling for more agile, transparent and responsive regulations to improve the business environment in Canada.

**Unaddressed patentee questions**

In February 2018, the PMPRB Board deferred a meeting request from industry, noting that the PMPRB was at that time preparing formal consultation sessions on the proposed Guideline reforms. To date, there have been no formal Guideline consultations, but rather the problematic SC and TWG processes that inadequately addressed stakeholder questions and concerns.

As part of the SC process, the industry submitted numerous questions critical to our collective understanding and engagement on the proposals. These questions were not answered by the PMPRB representatives.[9] We highlight this to help illustrate the questionable purpose of the SC, which did not provide clarity nor play a practical role in steering any workstreams. As such, the SC and TWG processes are not a substitute for robust Guideline consultations.

**Changes may jeopardize a regime that functions through voluntary compliance**

As an internationally unique quasi-judicial regime, the PMPRB has managed its role in large measure due to established Guidelines that promote voluntary compliance rather than frequent Board hearings. The vast majority of product issues are scrutinized and resolved between companies and PMPRB staff *before* a hearing becomes necessary. The regime proposed in *Canada Gazette Part I*, and as interpreted by the PMPRB staff throughout the SC process, places that balanced approach at risk.

Pharmacoeconomic value assessments may be useful as a tool to inform payor decision making (for example, as currently used by CADTH and INESSS) but they are inappropriate for regulatory purposes in a quasi-judicial context. Similarly, market size is a payor concern not directly related to excessive price ceilings. In addition, the proposed changes do not reflect a truly risk-based approach to how the PMPRB regulates ceiling prices that simplifies and streamlines compliance for patentees. IMC is concerned that the vision for the implementation of new regulatory factors as articulated during the SC process may have the opposite effect. Indeed, it was noted during the SC process that the PMPRB had obtained additional resources should patentees wish to "test" the new system. In IMC's view, and in the interest of all stakeholders, the new system should be designed to avoid unnecessary adversarial processes and outcomes.

As noted above, IMC's original meeting request in February 2018 was deferred in light of the ongoing consultation processes that have now concluded. IMC therefore reiterates its request that the PMPRB Board engage in a direct discussion with our industry regarding the many feasibility and implementation issues that have been identified to date, prior to any potential enactment of regulatory changes or the issuance of draft Guidelines.

[9] For example, see the questions posed by IMC on July 13, 2018; and the March 29, 2019, BIOTECanada and IMC Questions and Comments to Steering Committee Regarding the Technical Working Group Report).

Please do not hesitate to contact me if you have any questions, and I look forward to hearing from you regarding our meeting request.

Sincerely,

Pamela C. Fralick
President

cc: Doug Clark, Executive Director, PMPRB

Tanya Potashnik, Director, Policy & Economic Analysis Branch, PMPRB

Patented Medicine Prices Review Board Canada
Conseil d'examen du prix des médicaments brevetés Canada

Box L40, Standard Life Centre
333 Laurier Avenue West
Suite 1400
Ottawa, Ontario
K1P 1C1

**PROTECTED B**

June 27, 2019

Pamela C. Fralick
President
Innovative Medicines Canada
55 Rue Metcalfe Street
Suite/bureau 1220
Ottawa, ON
K1P 6L5

**Re: IMC Comments on the PMPRB Steering Committee and Technical Working Group Processes**

Dear Ms. Fralick,

Thank you for your letter dated May 27, 2019, expressing concern with aspects of the PMPRB's consultative process on guidelines modernization. I would like to thank you for taking the time to share your views and also for Innovative Medicines Canada's (IMC) continuing participation in that process. In responding to your concerns, I have sought to address them in roughly the same order as they appear in your letter.

I would first like to address your general concerns with respect to the process and outcome of the Steering Committee and Technical Working Group exercises. As the regulator responsible for giving effect to Health Canada's proposed amendments to the *Patented Medicines Regulations*, the PMPRB's role at this stage in the process is to conceive a new administrative framework that is fair, functionally sound and rationally connected to the nature and scope of the proposed regulatory changes. Given that the regulations have not been finalized and that there is always the possibility of changes being made between prepublication in Canada Gazette Part I and final publication in Part II, our objective in striking the Steering Committee and Technical Working Group at this stage was to seek preliminary feedback from stakeholders and experts at a fairly high level on a framework for an eventual set of new guidelines. As such, it was not our intent at this point in the process to delve into many of the more operational issues you touch on in your letter.

I can assure you, however, that if the regulations are eventually passed, these issues will be the subject of extensive consultation with groups and individuals who possess the requisite knowledge and expertise to help develop administratively feasible solutions that are minimally invasive for patentees. This approach is consistent with successful consultations we have conducted in the past.

In so far as the final report of the Technical Working Group is concerned, as you know, it contained 23 recommendations, each of which was adopted following a vote of members. The majority of the recommendations had unanimous support, and all were supported by at least three quarters of Working Group members. Each and every member had an opportunity to contribute to the discussions, to suggest modifications to the draft recommendations, and to propose revisions to the draft report prior to its finalization. As a group of technical experts, the purpose of the Working Group was not to comment on the policy intent behind the proposed regulatory changes or the new framework. This is made clear throughout the report and is reflected in its recommendations. The external reviewer noted that "the guidance and advice offered to the PMPRB seems appropriate and well balanced", while the two industry representatives on the Working Group observed that the Chair executed his mandate "as impartially as possible".

Regarding the question of what is the appropriate perspective to take when considering cost effectiveness, the text of Health Canada's Regulatory Impact Assessment Statement (RIAS) clearly points to a policy intent that is healthcare system focused: "affordability, accessibility and appropriate use of prescription drugs **to better meet health care system needs**" (my emphasis). To the extent possible, the PMPRB intends to rely on established and recognised processes, such as CADTH and INESSS, and not to consider perspectives that are not supported by such processes. Should the final regulations contain language that suggests a departure from this policy intent, the question of perspective will be revisited and consulted on further by the PMPRB.

On the matter of reporting confidential discounts, the framework proposed by the PMPRB contemplates a transparent list price ceiling for all new patented medicines but reserves a lower confidential ceiling price (the "MRP") for high priority medicines only. This is very much in line with the current global pharmaceutical pricing environment. As is the case today, the PMPRB would continue to abide by its *Patent Act* obligations to respect the confidentiality of pricing information provided by patentees. The initial proposal to use net confidential prices to set maximum transparent list prices for subsequent competitors has been abandoned by the PMPRB in response to concerns raised by industry stakeholders.

While I understand your concern regarding the average therapeutic class comparison for Category 2 medicines, especially in a market with low-priced generic competitors, please bear in mind that the approach described in the PMPRB's proposed framework would temper its impact through the application of a price floor based on the lowest price in the PMPRB12.

As for the case studies shared with the Steering Committee, these were intended to provide members with notional, high-level examples of how the guidelines might apply to Category 1 drugs. We anticipate that the majority of drugs under the PMPRB's jurisdiction will not fall into this category. Nonetheless, the price reductions identified in the case studies align with projections in Health Canada's cost benefit analysis (CBA) that accompanied the proposed regulations in Part I of the Canada Gazette and have been independently reviewed and validated by Dr. David Dodge.

Finally, the PMPRB remains committed to its longstanding policy of encouraging voluntary compliance. That is why the framework as proposed seeks to streamline compliance for patentees by applying bright line tests, such as a single cost effectiveness threshold for all Category 1 medicines and a fixed price ceiling for Category 2 medicines that is not recalculated

annually based on the previous year's average transaction price, as is currently the case. As with any significant change in the law, we do expect an increase in litigation as regulated parties test the boundaries of the new regime, but that is not the long term intent of the reforms.

I trust that the foregoing is responsive to your concerns. Should you wish to discuss any of these matters further, as always, PMPRB officials would be please to meet with you at your convenience. In the event the regulatory amendments are finalized in Part II of the Canada Gazette, the PMPRB will be communicating a timetable for next steps in the consultation process soon thereafter. We look forward to continued dialogue with IMC as that process unfolds.

Yours very truly,

Dr. Mitchell Levine
Chairperson, Patented Medicines Prices Review Board

# Patented Medicine Prices Review Board (PMPRB) Terms of Reference for Steering Committee on Modernization of Price Review Process Guidelines

## 1. Background

The PMPRB is consulting with its stakeholders on changes to its non-binding guidelines (the "**Guidelines**"), as contemplated by subsection 96(4) of the *Patent Act*. The purpose of these changes is to modernize the PMPRB's approach to carrying out its mandate to protect Canadian consumers from excessive patented drug prices. Two main types of changes are contemplated. The first type would operationalize Health Canada's proposed amendments to the *Patented Medicines Regulations* in order to make patented drugs more affordable for Canadians. The second would enable the PMPRB to make more efficient use of its resources by adopting a risk-based approach to how it regulates drug prices that simplifies and streamlines compliance for patentees.

The mandate of the Steering Committee is to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of new draft Guidelines that would give effect to these changes. This work will be based in part on the analysis and recommendations of a technical Working Group (the "**Working Group**") which will examine certain issues that the Steering Committee believes would benefit from the review of experts in health technology assessment and other economic and scientific matters.

A report of the Steering Committee's deliberations will be produced by PMPRB staff, which will be considered by the Board prior to the publication of new draft Guidelines for broader stakeholder consultation in the fall. This will result in a more focused and efficient consultation process.

Any analysis or recommendations emanating from the Working Group's review or from the Steering Committee's deliberations will not be binding on the Board.

## 2. Composition of the Steering Committee

The Steering Committee will be jointly chaired by the PMPRB's Director of Policy and Economic Analysis and the Director of Regulatory Affairs and Outreach. In addition to the co-chairs, the Steering Committee will consist of up to 17 members. Representatives from Health Canada and Innovation, Science and Economic Development (ISED) will also be present as observers. PMPRB Staff will attend meetings in order to provide administrative and other support, as required, to the Steering Committee. The members of the Steering Committee are identified below:

| Name | Title |
|---|---|
| Suzanne McGurn | Assistant Deputy Minister, Ontario Public Drug Programs Division, Ontario Ministry of Health and Long Term Care<br><br>Member - Jurisdictional (Ontario) and Vice-Chair of the Board, CADTH |
| Mitch Moneo | Assistant Deputy Minister, Pharmaceutical Services Division, Ministry of Health, British Columbia<br><br>Member - Jurisdictional (Western Provinces), CADTH |
| Susan Pierce | Manager, Pharmacy Policy Development Division, Department of Indigenous Service Canada |
| Scott Doidge | Director General, Non-insured Health Benefits – Department of Indigenous Service Canada |
| Dr. Robin McLeod | VP, Clinical Programs and Quality Initiatives, Cancer Care Ontario |
| Brian O'Rourke | President and Chief Executive Officer, Canadian Agency for Drugs and Technologies in Health (CADTH) |
| Dr. Luc Boileau | President and Chief Executive Officer, Institut national d'excellence en santé et en services Sociaux (INESSS) |
| Stephen Frank | President and CEO,<br>Canadian Life and Health Insurance Association (CLHIA) |
| Pamela Fralik | President, Innovative Medicines Canada |
| Declan Hamill | Vice-President, Legal, Regulatory Affairs and Compliance, Innovative Medicines Canada |
| Laurene Redding | Director Pricing, Contracting and Negotiations AstraZeneca, BioteCanada |
| Durhane Wong-Rieger | President and CEO, Canadian Organization for Rare Disorders |

| | |
|---|---|
| Dr. Jeff Blackmer | Vice-President, Medical Professionalism, Canadian Medical Association |
| Glen Doucet | Interim CEO, Canadian Pharmacists Association |
| Gail Attara | President and CEO of the Gastrointestinal Society, Best Medicines Coalition |
| Martine Elias | Director, Access, Advocacy and Communications Relations, Myeloma Canada |
| Jim Keon<br><br>Jody Cox (Alternate) | President, Canadian Generic Pharmaceutical Association (CGPA) and President, Biosimilars Canada<br><br>Vice-President Federal & International Affairs, CGPA |

| Observers | Title |
|---|---|
| Karen Reynolds | Executive Director, Office of Pharmaceuticals & Management Strategies, Health Canada |
| Eric Dagenais | Assistant Deputy Minister, Innovation, Science and Economic Development Canada |
| Imran Ali | Senior Manager, pan-Canadian Pharmaceutical Alliance Office |
| Rodrigo Arancibia | Deputy Director, Innovation, Policy and Integration |
| Declan Hamill | Vice-President, Legal, Regulatory Affairs and Compliance, Innovative Medicines Canada |
| Paul Petrelli | General Manager, Jazz Pharmaceuticals |

## 3. Function of the Steering Committee

The function of the Steering Committee is to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of the PMPRB's new, risk-based approach to regulating patented drug prices. This work will be informed in part by the analysis and recommendations of the Working Group, as per section 8 of these Terms of Reference and Appendix "A". A report of the Steering Committee's deliberations, and any associated advice or recommendations emerging from those deliberations, will be prepared by PMPRB staff for the Board's consideration.

## 4. Governance and procedure

It is recognized that the Steering Committee is composed of members who represent organizations with divergent and even diametrically opposed points of view on the policy rationale for the proposed amendments to the *Patented Medicines Regulations* upon which the Guideline changes are partly based. Members who represent organizations that are opposed to that policy are nonetheless encouraged to work constructively with the Steering Committee in carrying out its function.

The co-chairs are expected to foster consensus among members but, in order to ensure that Steering Committee deliberations are as focused and productive as possible having regard to the divisive nature of the underlying policy, they shall have final say on all matters of governance and procedure. Members who disagree with a decision of the co-chairs in this regard, can request that their objection be noted on the record. The co-chairs shall make every effort to ensure that the Steering Committee's final report accurately reflects any important points of convergence or contention between members.

## 5. Meetings

All Steering Committee meetings will take place at PMPRB offices in Ottawa.

The co-chairs will direct the work of the Steering Committee including calling for meetings and addressing any related scheduling issues.

An initial meeting of the Steering Committee will be held on June 25, 2018. Further meetings will be scheduled as required and, to the greatest extent possible, at dates and times to coincide with the availability of the members. It is anticipated that four meetings will be held in all, the first and last in person in Ottawa and the remainder by conference call or webinar.

## 6. Confidentiality

Steering Committee members may consult with their respective organizations on an ongoing basis but are expected to maintain the confidentiality of any materials specifically designated as confidential provided to them by PMPRB Staff during the course of their work. The names of the members of the Steering Committee will be published on the PMPRB's website along with a report of its deliberations and the analysis and recommendations of the Working Group.

## 7. Budget

The PMPRB may cover reasonable travel and accommodation costs of members where such funding is requested and approved in advance. Where possible, the co-chairs of the Steering Committee will arrange meetings to attempt to minimize expenditures for participants.

## 8. Establishment of Working Group

The PMPRB will establish a Working Group which will provide analysis and recommendations on certain matters that the Steering Committee believes would benefit from expert review. Further information on the Working Group can be found in Appendix "A".

# Terms of Reference for Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines

## Background

The Patented Medicine Prices Review Board (PMPRB) recently established a 'Steering Committee on Modernization of Price Review Process Guidelines'. The mandate of this **Steering Committee** is to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of the PMPRB's new draft Guidelines.

The Steering Committee's work will be based in part on the analysis and recommendations of a technical **Working Group**, which will examine certain issues that the Steering Committee believes would benefit from the review of experts in health technology assessment and other economic and scientific matters.

The Working Group will comprise leading experts in pharmacoeconomics and the clinical evaluation of pharmaceuticals. The Working Group will meet twice in-person and multiple times via tele-conference between July and October 2018. A report of the Working Group's deliberations and recommendations will be produced by the chair and submitted to the Steering Committee for consideration in October 2018.

## Membership

The chair of the Working Group will be Dr Mike Paulden (University of Alberta).

Thirteen individuals will sit as members of the Working Group (listed alphabetically):

1. Sylvie Bouchard (Patrick Dufort as alternate if needed) (INESSS);
2. Dr Chris Cameron (Dalhousie University and Cornerstone Research Group);
3. Dr Tammy Clifford (University of Ottawa and CADTH);
4. Dr Doug Coyle (University of Ottawa);
5. Don Husereau (University of Ottawa);
6. Dr Peter Jamieson (University of Calgary);
7. Dr Frédérick Lavoie (Pfizer Canada);
8. Dr Karen Lee (University of Ottawa and CADTH);
9. Dr Christopher McCabe (University of Alberta and Institute of Health Economics);
10. Dr Stuart Peacock (Simon Fraser University and BC Cancer Agency);
11. Maureen Smith (Patient);
12. Geoff Sprang (Agmen);
13. Dr Tania Stafinski (University of Alberta).

Two individuals will sit as observers of the Working Group:

1. Edward Burrows (Innovation, Science and Economic Development);
2. Nelson Millar (Health Canada).

One individual will act as an external reviewer of the Working Group's draft report:

1. Dr Mark Sculpher (University of York).

Recommendations of the Working Group will be determined by a vote of the members. In the event of a tie, the chair will have the casting vote.

# Areas of focus

The Working Group will examine and make recommendations with respect to the following considerations and questions:

**1. Options for determining what medicines fall into 'Category 1'**

- A Category 1 medicine is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing.

- The following criteria have been identified as supporting a Category 1 classification:

    a) The medicine is 'first in class' or a 'substantial' improvement over existing options
    b) The medicine's opportunity cost exceeds its expected health gain
    c) The medicine is expected to have a high market impact
    d) The medicine has a high average annual treatment cost

- Should other criteria be considered? What are the relevant metrics for selecting medicines that meet the identified criteria and what options exist for using these metrics?

**2. Application of supply-side cost effectiveness thresholds in setting ceiling prices for Category 1 medicines**

- Potential approaches for implementing a price ceiling based on a medicine's opportunity cost.

- Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc)

**3. Medicines with multiple indications**

- Options for addressing medicines with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).

**4. Accounting for uncertainty**

- Options for using the CADTH and/or INESS reference case analyses to set a ceiling price.

- Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.

**5. Perspectives**

- Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a 'significant' difference between price ceilings under each perspective.

- How to define a 'significant' difference in price ceilings between each perspective.

**6. Application of the market size factor in setting ceiling prices**

- Approaches to derive an appropriate affordability adjustment to a medicine's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' approach).

Additional areas of focus may be identified by the Steering Committee prior to the first meeting of the Working Group in July 2018.

It is anticipated that the approaches or methods recommended by the Working Group may not be identical to approaches or methods currently employed by CADTH or INESSS. Where such departures present potential hurdles for operationalization of its recommendations, the Working Group will identify potential technical or other solutions to these hurdles.

## Confidentiality

Working Group members may consult with non-members on an ongoing basis but are expected to maintain the confidentiality of any materials provided to them during the course of their work.

The names of the members of the Working Group will be published on the PMPRB's website, along with a report of its deliberations, analysis and recommendations.

## Governance and procedure

It is recognized that members of the Working Group may hold opposing points of view on the above issues and/or disagree with the policy rationale underlying the changes to the PMPRB's Guidelines. Members are nonetheless encouraged to work together constructively to assist the Working Group in carrying out its function.

The chair is expected to foster consensus among members, but in order to ensure that Working Group deliberations are as focused and productive as possible, the chair shall have final say on all matters of governance and procedure. Members who disagree with a decision of the chair in this regard can request that their objection be noted on the record. The chair shall make every

effort to ensure that the Working Group's final report accurately reflects any important points of convergence or contention between members.

## Schedule

The Working Group will meet for the first time in-person in Ottawa in July, followed by numerous tele-conferences in August and September. Following submission of a draft report, a second in-person meeting will be held in October.

All dates are subject to the availability of the chair and members of the Working Group.

| **Date** | **Event** | **Purpose** |
|---|---|---|
| 26 July 2018 | Full day in-person meeting in Ottawa | Overview of Working Group objectives. Summary of specific areas of focus under consideration. Allocation of tasks among Working Group members. |
| 22-24 August 2018 | One-hour teleconference on each area of focus | Opportunity for input from Working Group members. |
| 24 August 2018 | Two-hour tele-conference | Update on Working Group status. Opportunity for input from Working Group members. |
| Week of 10 September or 24 September 2018 (TBC) | Two-hour tele-conference | Update on Working Group status. Opportunity for input from Working Group members. |
| 5 October 2018 | Draft report circulated among PMPRB staff and Working Group members | Opportunity for input from PMPRB and Working Group members. |
| 12 October 2018 | Full day in-person meeting in Ottawa | Present draft report. Report draft recommendations. Final opportunity for input from PMPRB and Working Group members. |
| 26 October 2018 | Final report delivered to PMPRB | Final deliverable to PMPRB. |

## Deliverables

A draft report will be circulated among PMPRB staff and Working Group members on 5 October 2018, prior to the final in-person meeting in Ottawa. A final report will be submitted to the PMPRB on 26 October 2018 and circulated among Working Group and Steering Committee members.

Following delivery of the final report, the chair will be willing to present the recommendations of the Working Group to stakeholders and other interested parties, subject to availability.

## Budget

The PMPRB may cover reasonable travel and accommodation costs of members where such funding is requested and approved in advance. Where possible, the chair of the Working Group will arrange meetings to attempt to minimize expenditures for participants.

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# PMPRB Framework Modernization

***Presentation to Steering Committee***
***June 25, 2018***

Canada

# Outline

- Background on Guideline reform
- Objectives and guiding principles
- Outline of new Guidelines framework
- Technical Working Group and Next Steps

# The Government of Canada is committed to making prescription drugs more affordable

"A Liberal government's... priorities for a new Health Accord will include:

We will consult with industry and review the rules used by the Patented Medicine Prices Review Board to ensure value for the money governments and individual Canadians spend on brand name drugs."


JUSTIN TRUDEAU,
PRIME MINISTER OF CANADA

**Minister of Health Mandate Letter**

- improve access to necessary prescription medications. This will include joining with provincial and territorial governments to negotiate common drug prices, reducing the cost Canadian governments pay for these drugs, making them more affordable for Canadians, and exploring the need for a national formulary;

Government of Canada / Gouvernement du Canada

Home → Health → Health system and services → Health-related consultations → Consulting on Proposed Amendments to the Patented Medicines Regulations

**Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations**

Government of Canada / Gouvernement du Canada

Home → Budget 2017 → Budget Plan

**Chapter 3 – A Strong Canada at Home and in the World**

**Prescription Medications and Health Innovation**

To promote a more innovative health care system, Budget 2017 proposes measures that include:

- Improving access to prescription medications, lowering drug prices and supporting appropriate prescribing through an investment of $140.3 million over five years, starting in 2017–18, with $18.2 million per year ongoing, for Health Canada, the Patented Medicine Prices Review Board and the Canadian Agency for Drugs and Technologies in Health.

CBC | MENU

**Ontario Health Minister Eric Hoskins to chair newly created federal pharmacare committee**

Hoskins resigns as provincial health minister

Vik Adhopia · CBC News · Posted: Feb 26, 2018 4:38 PM ET | Last Updated: February 26

# Reform of federal drug price regime long overdue

- The PMPRB and its regulatory framework were designed at a time before the Internet or cell phones
- Built to respond to changing intellectual property standards of the mid-1980s, price protection for patentees was seen as a good trade-off for attracting R&D
- Price ceilings were based on pricing data that was public and compared against the highest R&D jurisdictions in the hopes of emulating them
- In the 30 years since, the anticipated benefits haven't materialized and the regulatory pricing model is broken

## Assessing Canada's Patented Drug Pricing Regulations

Original design and intent vs. current realities

Designed to respond to realities of the mid-1980s

- Changes to IP and price regimes in exchange for increased domestic R&D investment
- Price ceilings based on public list prices that reflect market prices
- Market dominated by small molecule drugs indicated for more common ailments

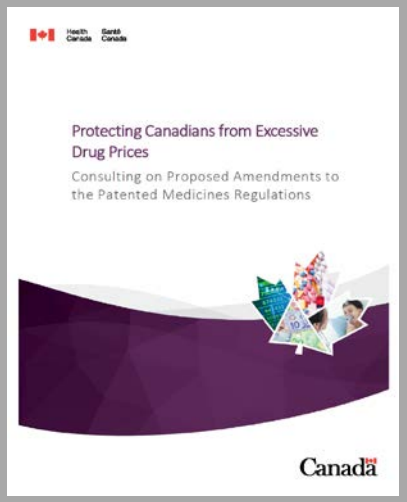
Like any technology intensive industry, pharma has evolved significantly

- Higher prices and a decline in domestic R&D investment
- Confidential rebates and inflated list prices
- Specialized biologic and genetic therapies are fastest growing drug classes

# We've been consulting since June 2016

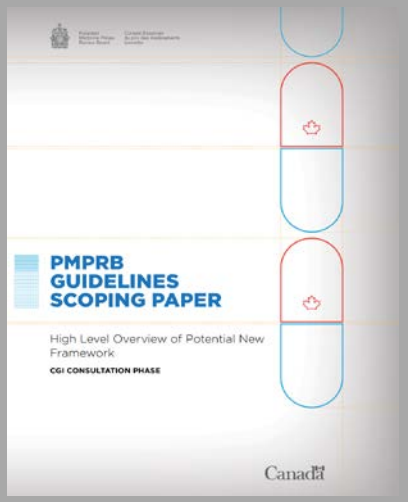
**PMPRB Discussion paper on Guideline reform**


**Health Canada pre-consultation on regulatory amendments**




**Health Canada Gazette 1**


**PMPRB Guidelines scoping paper**

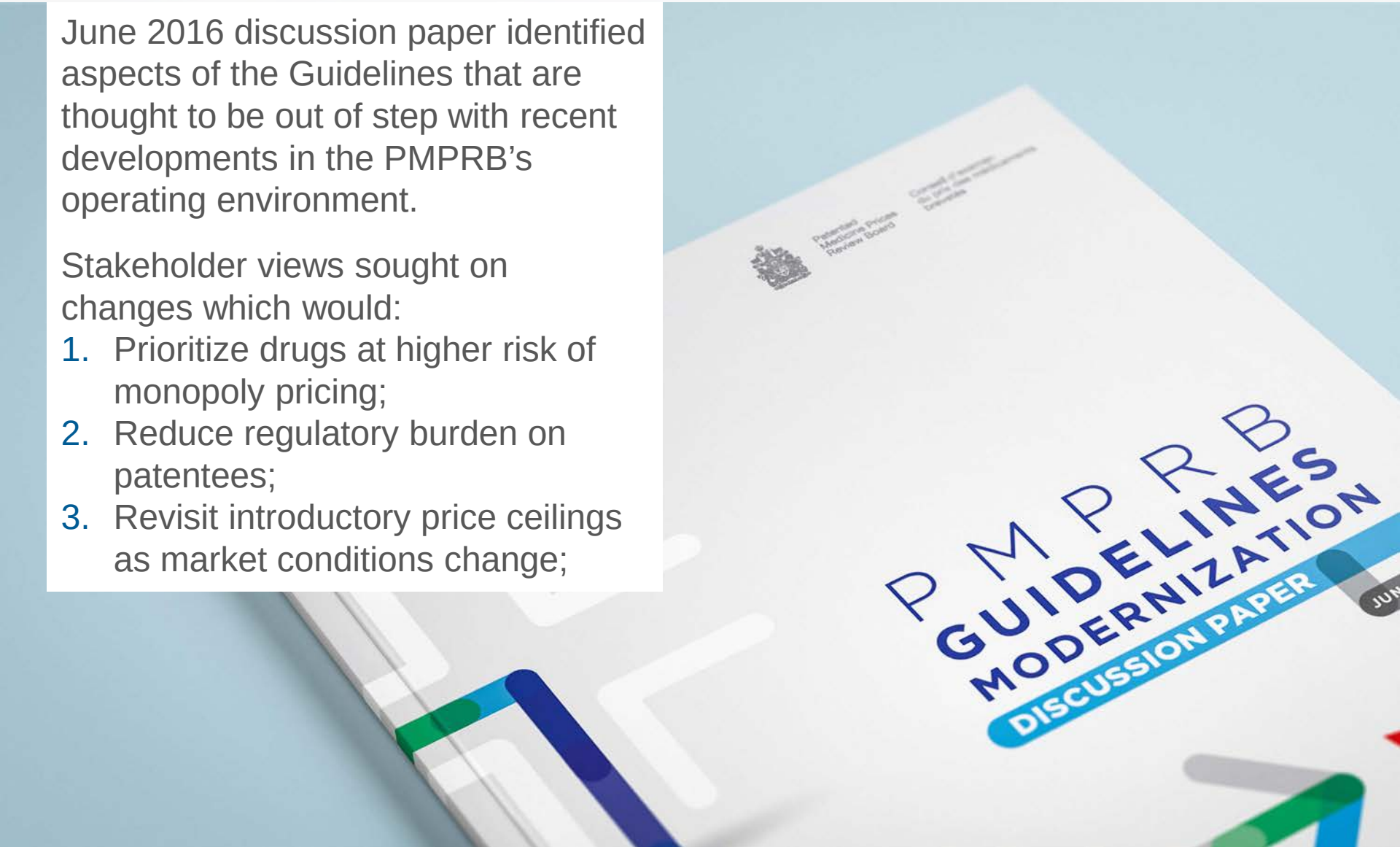


# PMPRB discussion paper on Guideline reform

June 2016 discussion paper identified aspects of the Guidelines that are thought to be out of step with recent developments in the PMPRB's operating environment.

Stakeholder views sought on changes which would:

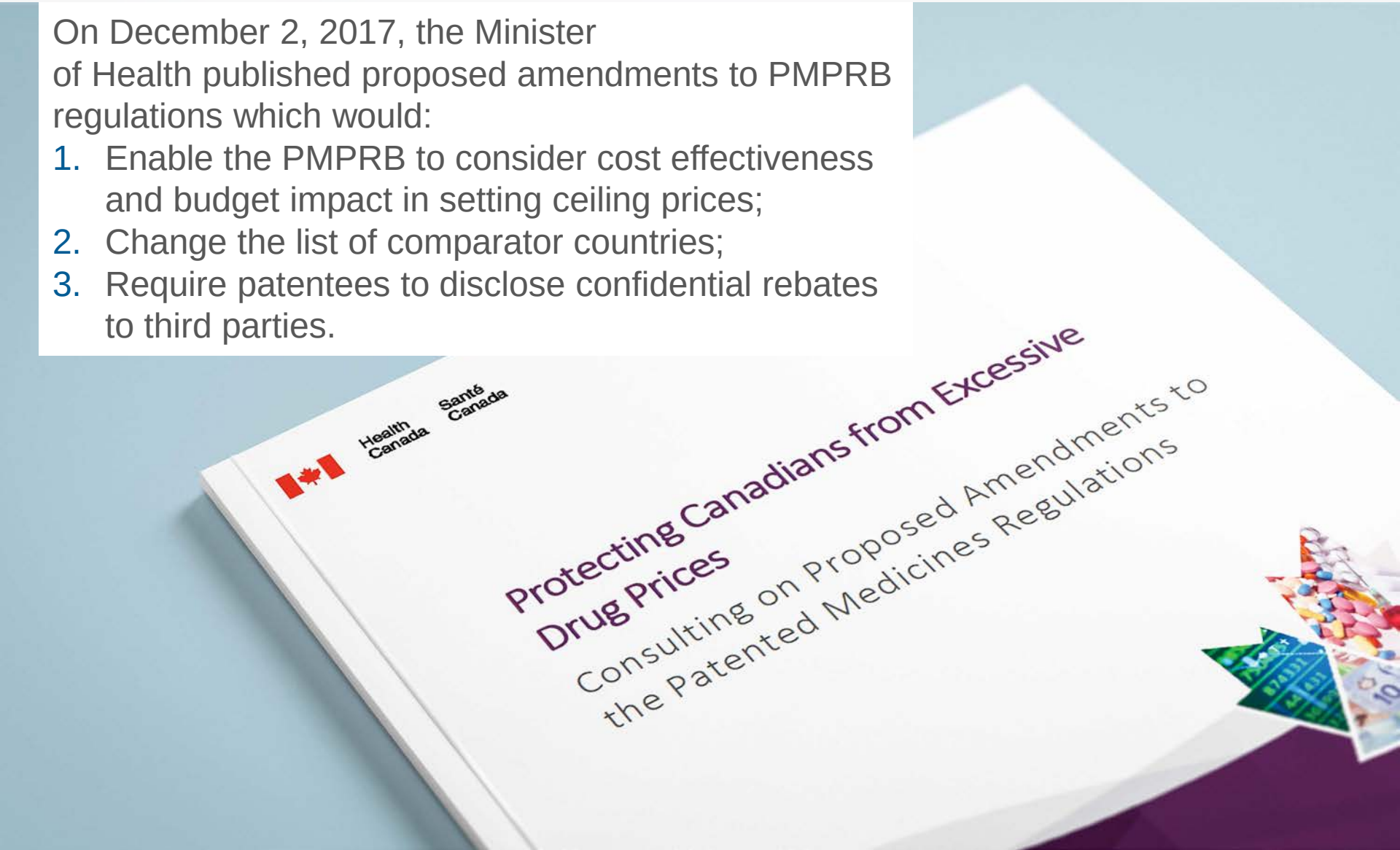
1. Prioritize drugs at higher risk of monopoly pricing;
2. Reduce regulatory burden on patentees;
3. Revisit introductory price ceilings as market conditions change;



# Health Canada proposed regulatory amendments

On December 2, 2017, the Minister of Health published proposed amendments to PMPRB regulations which would:

1. Enable the PMPRB to consider cost effectiveness and budget impact in setting ceiling prices;
2. Change the list of comparator countries;
3. Require patentees to disclose confidential rebates to third parties.



# Latest step: Steering Committee

- The Steering Committee is being asked to provide targeted stakeholder feedback on key features of a new Guidelines framework which will serve the following dual objectives:

1. Operationalize amendments to the Patented Medicines Regulations designed to lower patented drug prices; and,
2. Support a risk-based approach to regulating drug prices that simplifies and streamlines compliance for patentees.

- In deliberating on the above, the Steering Committee should seek to strike a balance between the following guiding principles:
  - Sustainability
  - Predictability
  - Consistency
  - Functionality
  - Fairness
- The Steering Committee will be assisted by a technical Working Group (the "**Working Group**") with expertise in health technology assessment and other economic and scientific matters.

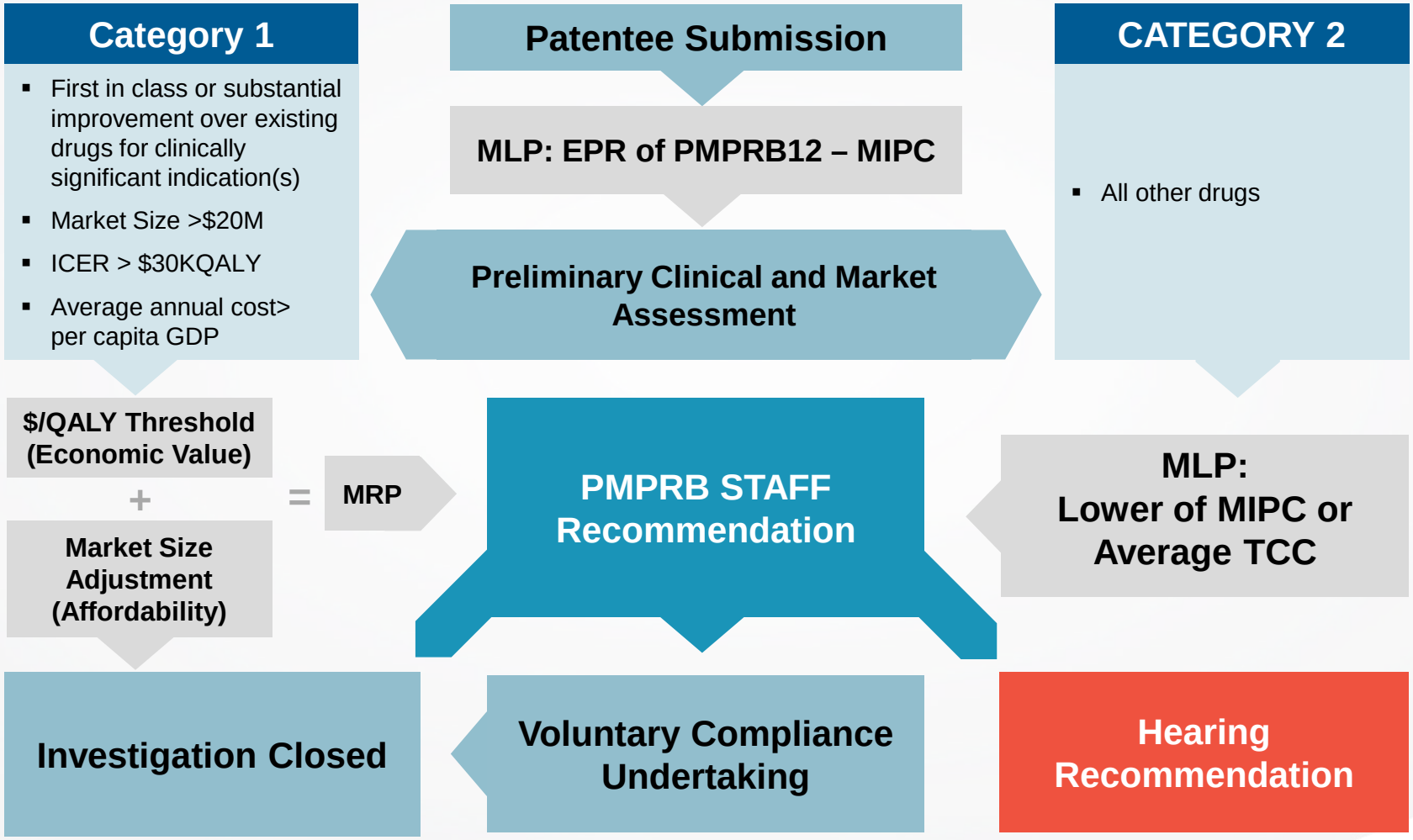
# Suggested questions for Steering Committee

- Is the proposed division and treatment of Category 1 and Category 2 drugs a reasonable risk-based regulatory approach?
- Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?
- Should exceptions be made to the MLP-MIPC test and, if so, when and why?
- Should there be a price floor for Category 2 drugs based on LIPC?
- Should further drug categories exist with different treatment modalities from those proposed?
- Should more or less criteria be considered in screening a drug as higher risk and, where should the line be drawn with respect to the criteria?
- Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?
- Should Category 2 drugs be scrutinized more or less than proposed?
- Should the cost effectiveness threshold for Category 1 drugs vary?
- Should a Category 1 drug ever have more than one MRP?
- Are there economic considerations that would support a higher MRP for some Category 1 drugs than would result from the proposed application of the new factors?
- How often and in what circumstances should a drug be rebenched?
- Should confidential third party pricing information only be used for compliance purposes?
- Is there a better way to deal with existing drugs under the new framework?
- Are there opportunities to further reduce regulatory burden while respecting the dual objectives?

# Overview of new Guidelines framework

- A risk-based approach to price regulation that considers value and affordability, in addition to list prices in other like-minded countries.
- Basic structure can be broken down into 5 parts:
  - Part I: ‘Maximum List Price’ (MLP) for all new drugs at introduction based on median of PMPRB12 (MIPC)
  - Part II: Screening of drugs into high priority (Category 1) or low priority (Category 2)
  - Part III: ‘Maximum Rebated Price’ (MRP) for Category 1 drugs based on new pharmacoeconomic, market size and GDP factors
  - Part IV: Lower of MIPC and average of Therapeutic Class (ATCC) for Category 2 drugs
  - Part V: Re-benching
- The MLP will be a transparent ceiling based on public list prices but the MRP, which applies to Category 1 drugs only, will be confidential.
- To comply with the MRP, patentees of Category 1 drugs will be required to submit information on undisclosed rebates to third parties.

# Proposed PRICE Review Schematic



# Old vs new regime…

| Rule | How The Current Regime Works | How The Updated Regime Would Work |
|---|---|---|
| **How international prices affect maximum prices in Canada** | A new and improved drug cannot be priced higher than the median price of that same drug in the PMPRB7 | All new drugs cannot be priced higher than the median price of that same drug in the PMPRB12 |
| **How domestic prices affect maximum prices in Canada** | A new drug that isn't an improvement over existing drugs cannot be priced higher than the highest priced existing comparator drug in Canada | A new drug that isn't an improvement over existing drugs cannot be priced higher than the lower of the average price of existing comparator drugs in Canada and the median of the PMPRB12 |
| **How inflation affects maximum prices in Canada** | The price of a drug can increase every year with inflation. However, if a drug's price decreases in one year, its ceiling price the next year will be constrained by that decrease in price. | The ceiling price of a new drug is fixed at introduction. Prices can vary freely below this level in subsequent years.<br>. |
| **Changes to the maximum ceiling price after a new drug enters Canada** | Once a new drug is given its ceiling price, it can only change through inflation or if the drug company voluntary lowers it. | The maximum price may be rebenched after a few years based on specific changes in market conditions. |

# Old vs new regime (continued)

| Rule | How The Current Regime Works | How The Updated Regime Would Work |
|---|---|---|
| **Pharmacoeconomics** | How much a drug costs for the amount of benefit it provides (e.g., $100 a pill for a year of healthy life) is not considered by the PMPRB in setting a maximum price | The cost-effectiveness of Category 1 drugs in terms of cost per quality-adjusted life year (QALY) is assessed against an evidence based threshold |
| **Market size and GDP*** | The total amount of money available to be spent on new drugs every year is not considered by the PMPRB in setting a maximum price | The market size of a new drug is a function of how much it costs and how many patients will need it. Drugs that are expected to have a significant market size and impact on the healthcare system will have a lower ceiling price to deter rationing. |

*Each year, the amount of money available to be spent on new drugs depends on total spending on drugs the year before and how much the economy is growing. For example, if Canada spent $1000 on drugs in 2018 and its economy grew by 2%, it would have $20 more to spend on the new drugs that come to market in 2019 (for a total of $1020)

# Part 1:Median international price test (MIPC)

- All new drugs are assigned a Maximum List Price (MLP) based on the median of the PMPRB 12 (MIPC).
- IMS will be used to verify international list prices.
- Category 1 drugs will be given both an MLP based on the MIPC and a Maximum Rebated Price (MRP)
- All other drugs will be deemed Category 2 and have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- No Category 2 drug will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).

# Part II: Screening

- Drugs will be screened into Category 1 if they are:

1. First in class or substantial improvement over existing therapy
2. Expected to have sales in excess of a $20 million/year market size threshold
3. Above a $30K/QALY threshold for clinically significant indications
4. Have an average annual treatment cost above per capita GDP.

# Part III: MRP for Category 1 drugs

- Step 1: application of pharmacoeconomic factor
  - Empirical work undertaken by Karl Claxton at the University of York suggests a $30K/QALY opportunity cost threshold for Canada.
  - PMPRB will use this estimate at the screening phase to determine whether a drug should go in Category 1 or Category 2.
  - Category 1 drugs will then be subject to a baseline maximum value-based price ceiling of $60K/QALY, for reasons of practicality and efficiency.
  - Drugs that meet certain clinical characteristics (e.g., high burden of disease or significant absolute gain in QALY) may be subject to a higher $/QALY ceiling.

# Part III: MRP for Category 1 drugs (continued)

- Step 2: application of market size and GDP factors
  - A Category 1 drug that meets the applicable $/QALY ceiling may still face an adjustment in price if the application of the market size and GDP factors raise affordability concerns.
  - Using new drug contribution to GDP and GDP growth over the last five years, the PMPRB is estimating a threshold of $20M per new drug.
  - New Category 1 drugs with an estimated market size that exceeds this threshold within any of its first five years of sale will require further price adjustments.
  - The adjustment would see the MRP reduced by a certain percentage discount which would increase as the expected market size increases (see next slide).
  - The $20M threshold would also increase annually based on GDP growth and/or CPI.

# Application of new factors to Category 1 drugs

| Type of review | $/QALY target to set MRP | Market impact adjustment |
|---|---|---|
| **Baseline New Drug (market size up to $20M)** | $60K | N/A |
| **"Premium" New Drug (e.g. high burden, EDRD, significant absolute QALY gain)** | $90K to $150K | N/A |
| **High Impact New Drug (market size over $20M)** | $60K | 10% reduction on MRP for each additional $10M market size (to 50% maximum) |

# Part IV: MLP for Category 2 drugs

- As mentioned, Category 2 and have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- However, no Category 2 drug will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).

# Part V: Re-benching

- All new drugs will be given an interim MLP of 3 years or until the drug is sold in 7 countries, whichever comes first.
- MLP is then frozen, as is MRP, unless re-benching is triggered by one of the following criteria:
  - Approval of a new indication
  - Sales in excess of expected market size
  - New evidence on cost-effectiveness (e.g. CADTH therapeutic class review or lifting of HC conditions on NOC)
  - Significant changes in international prices (eg. MIPC < MIPC at intro by more than 25%)
- Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI

# How compliance with new price ceilings will be assessed

- Price reviews will be conducted for the following customer classes:
  - National Retail – list price assessed against MLP
  - National Private Payer – average transaction price (ATP) assessed against MRP
  - Provincial Public Payer – ATP assessed against MRP in each market
- ATPs are calculated net of all discounts to determine compliance with confidential MRP.
- Category 2 drugs will be assessed against MLP.

# How pricing complaints will be managed

Complaints received by the PMPRB will trigger an investigation, during which the PMPRB will assess whether:

1. a drug is in compliance with the Guidelines; and
2. whether circumstances in the market have changed to warrant a rebenching/reclassification.

# Application of new Guidelines to existing drugs

- Existing drugs will be given an interim price ceiling based on the MIPC of the PMPRB12.
- An existing drug will only be classified as Category 1 if it fails a $100K/QALY screen for any indication.
- Existing drugs that are screened into Category 1 will be prioritized for re-benching.
- Category 2 drugs will be re-benched later unless a complaint is received.
- All drugs within a therapeutic class will be assessed at the same time for the purposes of the ATCC test.
- Patentees will be advised in advance of re-benching and given two reporting periods to come into compliance.

# Reminder: suggested questions for Steering Committee

- Is the proposed division and treatment of Category 1 and Category 2 drugs a reasonable risk-based regulatory approach?
- Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?
- Should exceptions be made to the MLP-MIPC test and, if so, when and why?
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- Is there a better way to deal with existing drugs under the new framework?
- Are there opportunities to further reduce regulatory burden while respecting the dual objectives?

# Technical questions for analysis and recommendation by the Working Group

- The draft Terms of Reference for the Working Group identify the following issues:
    - The economic and scientific rationale for selecting specific criteria for screening drugs as high priority and associated metrics
    - How opportunity cost and willingness to pay should factor into the application of cost effectiveness thresholds
    - How to address drugs with multiple indications
    - How to make optimal use of CADTH and INESSS analyses and how to account for uncertainty in doing so
    - How to assess affordability by applying market size and GDP factors
- The Steering Committee has until July 13 to identify further issues it believes would benefit from expert review and analysis.

# Annex

# ICER calculations for Canada based on Patented drugs sales

| Item | Parameter | 2012 | 2013 | 2014 | 2015 | 2016 | Source |
|---|---|---|---|---|---|---|---|
| 1 | Growth in GDP 2014–15 (+1%) | 2.75% | 3.48% | 3.57% | 1.94% | 2.43% | OECD |
| 2 | Total Healthcare spending ($B) | $205.40 | $209.30 | $215.80 | $222.10 | $228.00 | CIHI |
| 3 | Contribution of patented medicines % | 6.43% | 6.50% | 6.53% | 6.80% | 6.80% | Calculation (Row 4 / Row 2) |
| 4 | Contribution of patented medicines ($B) | $13.20 | $13.60 | $14.10 | $15.10 | $15.50 | PMPRB |
| 5 | Annual threshold for net healthcare cost growth for all new patented medicines ($M) | $363 | $473.28 | $503.37 | $292.94 | $376.65 | Calculation (Row 1 X Row4) |
| 6 | Average number of patented medicines per year | 35 | 35 | 35 | 35 | 35 | PMPRB |
| 7 | Annual threshold of average cost growth per new patented medicine ($M) | $10.4 | $13.5 | $14.4 | $8.4 | $10.8 | Calculation (Row 5 / Row 6) |
| 8 | Annual threshold for estimated budget impact for each new patented medicine ($M) Multiplied by 2 | $20.7 | $27.0 | $28.8 | $16.7 | $21.5 | Calculation (Doubling of Row 7) |
| 9 | Annual threshold for estimated budget impact for each new patented medicine ($M) Multiplied by 3 | $31.1 | $40.6 | $43.1 | $25.1 | $32.3 | Calculation (Tripling of Row 7) |

# Assessing health opportunity costs for the Canadian health care systems

Ochalek J.[1], Lomas J.[1] and Claxton K.[1,2]

1. Centre for Health Economics, University of York

2. Department of Economics and Related Studies, University of York

12th March 2018

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**Summary**

The economic evaluation of health care interventions including new health technologies such as branded pharmaceuticals requires an assessment of whether the improvement in health outcomes they offer exceeds the improvement in health that would have been possible if the additional resources required had, instead, been made available for other health care activities. Therefore, some assessment of these health opportunity costs is required if the best use is to be made of the resources available for health care. It is this assessment of health opportunity costs that indicates the maximum that health care systems can afford to pay for the benefits offered by new drugs protected by patent. This represents the temporary monopoly price that could be paid if health care systems choose not to use their monopsony power and is consistent with price regulation that upholds the protections offered by existing patents.

This report provides a brief review of the literature on the assessment of health opportunity costs, outlines how existing estimates of the effect of changes in health expenditure on mortality, as well as survival and morbidity, can be used to provide some initial assessment of a cost-effectiveness threshold that reflects likely health opportunity costs across the different provinces of Canada. The range of possible estimates based on existing work are discussed and some suggestions are made of how further research could provide estimates that more closely reflect evidence of the health effects of health care expenditure in the Canadian provinces.

Based on the balance of the evidence currently available some recommendations can be made. There is a wide range of potential cost per DALY averted estimates for Canada ($20,000 to $100,000 per DALY averted in Table 4), with the lower estimates associated with more recent work using within country rather than country level data. Therefore, it is the lower end of this range that might be regarded as most plausible, so ***a cost per DALY threshold is likely to be less than $50,000 for Canada as a whole***.

A measure of heath benefit more appropriate to Canada would be QALY gained rather than DALYs averted. However, currently there are no estimates of QALY burden of disease which would allow estimates of the mortality effects of changes in expenditure to be used to estimate a cost per QALY threshold. Nonetheless, estimates of the DALYs averted from changes in expenditure are on average likely to be similar or less than the QALY gained. Therefore, ***a cost per QALY threshold is likely to be similar or lower than a cost per DALY averted threshold.***

This is consistent with the range of implied cost per QALY gained for Canada based on the analysis in Woods et al 2016. Estimates based on this analysis have been adopted in Norway while further research using within country data are explored. Using this approach would provide a cost per QALY threshold for Canada of $28,089.

Therefore, taking all this evidence together suggests that ***a cost per QALY threshold of $30,000 per QALY would be a reasonable assessment of the health effects of changes in health expenditure for Canada as a whole and is likely to be similar across most provinces***.

## 1. Introduction

Evidence of the expected costs and health effects of making a new health technology available to specific populations in a particular setting and health care system (HCS) are often summarised as incremental cost-effectiveness ratios (ICERs). These ratios are often expressed as the cost per Quality Adjusted Life Year (QALY) gained or the cost per Disability Adjusted Life Year (DALY) averted (Salomon et al. 2012). These measures provide a useful summary of how much additional resource is required to achieve a measured improvement in health (the additional cost required to gain one QALY or to avert one DALY). Whether the cost per QALY gained or DALY averted offered by an intervention is regarded as worthwhile requires a comparison with a cost-effectiveness 'threshold'. An effective intervention will only improve health outcomes overall (i.e., produce a positive net health benefit) if the additional health benefits exceed the health opportunity costs associated with the additional health care costs that must be found from existing commitments or that use additional expenditure that could have been devoted to other health care activities. Such an assessment of health opportunity cost reflects the maximum a HCS can afford to pay for the health benefits that a new health technology offers, without reducing health outcomes overall. Therefore, an evidence based assessment of health opportunity costs is critical to the appropriate pricing of new branded pharmaceuticals while they are protected by patent (Claxton et al. 2008; Claxton et al. 2011).

A cost per QALY 'threshold' that reflects the health opportunity costs of changes in health expenditure indicates the maximum that health care systems can afford to pay for the benefits offered by new drugs protected by patent. It represents the value of the innovation to the health care system, or the temporary monopoly price that could be paid while it is protected by patent. Therefore, establishing prices for new drugs based on an assessment of their health benefits and a cost per QALY threshold that reflects health opportunity costs is consistent with upholding the protections offered by patents. It does mean that the value of the innovation will be appropriated by the manufacturer in the short run before the patent expires. However, on patent expiry the health care system starts to appropriate the value of the innovation as cheaper generic versions of the original brand enter a competitive generics market. Prescribing can then switch to cheaper generic versions of the old brand and/or any new patented drugs that enter are compared to the cheaper generic versions of the old brand when establishing how much health care systems can afford to pay for the additional benefits they offer. Therefore, setting prices for new drugs that are protected by patent based on an assessment of health opportunity costs, only until the patent expires, ensures that the value of innovation is shared between manufacturers and health care systems in a way that is consistent with existing levels of patent protection.

### *Estimating health opportunity costs*

A persistent problem has been that the cost-effectiveness 'thresholds' (e.g. cost per QALY or cost per DALY thresholds) recommended or cited by decision making and advisory bodies (both national and supra-national) reflect a lack of conceptual clarity about what they ought to represent and what type of evidence might inform their assessment (Revill et al. 2014; Culyer 2016). As a consequence these values are not evidence based and have simply become established norms or implied values, which describe the criteria used to judge cost-effectiveness (Claxton, Sculpher, et al. 2015). Other proposed thresholds reflect a view of what value ought to be placed on improvements in health.

They imply what health care expenditure ought to be (the social demand for health) rather than an evidence based assessment of health opportunity costs given actual levels of expenditure, i.e. a 'supply side' estimate of the amount of health that a HCS currently delivers with more or less resources.

The problem of estimating a cost-effectiveness 'threshold' that represents expected health opportunity costs is the same as estimating the relationship between changes in health care expenditure and health outcomes. Estimates of the marginal productivity of health expenditure in producing health (QALYs) are becoming available for some high income countries based on approaches to estimation which exploit within country data (Martin et al. 2008; Vallejo-Torres et al. 2016; Edney et al. 2017; Claxton, Martin, et al. 2015). This evidence from national HCS contexts in high income countries can be used to give some indication of possible values in other contexts (Woods et al. 2016) based on estimates of the income elasticity of demand for health and assumptions about the relative underfunding of HCS (i.e., the shadow price for public expenditure on health). Another approach has taken estimates of the effect of health care expenditure on health outcomes based on country level data (typically expressed as elasticities) and applied these to country-level baseline health and demographic data to generate overall cost per DALY 'thresholds' (Ochalek et al. 2015).

Canada has a longstanding health technology assessment agency in CADTH that makes use of cost-effectiveness evidence in the form of ICERs. However, like in many other jurisdictions, there is no explicit and empirically-informed 'threshold' that reflects the likely health opportunity costs so it is not possible to assess the likely net health effect of approving a new health technology or establish what price ought to be paid for new pharmaceuticals protected by patent. Although Canada is similar to countries, such as the UK, in terms of the availability of high quality health and health care data, there are, as yet, no estimates of the marginal productivity of health care expenditure using Canadian data. In addition a significant difference exists between the HCS of Canada and the UK, in that decisions in Canada are more likely to be made, not at the national level, but at the level of individual provinces. This report details the methodology that was used to generate province-level estimates of health opportunity costs (cost per DALY 'thresholds'). In broad terms, this involved tailoring the approach taken by Ochalek et al. (2015) to consider health opportunity costs that occur at the provincial level using province specific data on health expenditure, epidemiology and demographics.

## 2. Methods

The effect of different levels of health care expenditure on mortality outcomes has been investigated in a number of published studies using country level data, many including high as well as low and medium income countries (Gallet & Doucouliagos 2017). The challenge is to control for all the other reasons why mortality might differ between countries to isolate the causal effect of differences in health expenditure (Nakamura et al. 2016). This is a particular challenge even if available measures are complete, accurate and unbiased because health outcomes are likely to be influenced by expenditure (increases in expenditure improves outcomes), but outcomes are also likely to influence expenditure (poor outcomes prompt greater efforts and increased expenditure). This problem of endogeneity, as well as the inevitable aggregation bias, risks underestimating the

health effects of changes in expenditure. Instrumental variables have been used in a number of studies to try and overcome this problem and estimate outcome elasticities for all cause adult, maternal and child mortality (Bokhari et al. 2007 among others). The Bokhari et al (2007) model specification applies an instrumental variable approach to cross-sectional data from the year 2000 for 127 countries and models both public expenditure on health and a country's GDP as endogenous variables (both in per capita terms). Specifically, the identification strategy of Bokhari et al (2007) employs two instrumental variables: military expenditure per capita of neighbouring countries and a measure of institutional quality. These represent typical instrumental variables following in the tradition of earlier papers such as Filmer & Pritchett (1999). In addition, Bokhari et al (2007) perform a logarithmic transformation of their data so that coefficients can be interpreted as elasticities, and allow for the outcome elasticity with respect to expenditure of countries to vary by two variables: the level of infrastructure (proxied by 'paved roads per unit of area') and shock in donor funding (measured by absolute deviation in current donor funding from historical mean).

This approach to estimation using country level data can provide country specific cost per DALY averted values by applying estimated elasticities, which take account of measures of a country's infrastructure and changes in donor funding, to country specific mortality rates, conditional life expectancies and population distribution (all by age and gender) as well as estimates of disability burden of disease and total health care expenditure. We re-estimate the effect of changes in expenditure using Bokhari et al (2007)'s dataset after expanding the dataset to include under-5 mortality from the World Bank in addition to adult male and adult female mortality, which enables greater coverage of the population, as well as: i) a measure of survival, years of life lost (YLLs); ii) a measure of morbidity, years of life disabled (YLDs); and iii) DALYs, a generic measure of overall ill health, from the Global Burden of Disease database. Although elasticities are estimated at the country level, they differ only with respect to the interaction of measures of infrastructure and donor funding. The estimated elasticities for Canada (see Table 2) are applied to province specific data on health expenditure, epidemiology and demographics, i.e., in the absence of elasticity estimates at the provincial level the estimate for Canada are assumed to be common across the provinces. Nonetheless, the health effects of changes in health expenditure will differ across provinces due to differences in health expenditure, epidemiology and demographics.

There are four ways in which the estimated elasticities in Table 2 can be used to estimate the likely DALYs averted as a consequence of a 1% change in health expenditure in each province, *i*. Each of the four ways in which a cost per DALY can be estimated are summarised in Table 1 and are briefly described below, with details of the data used reported in Appendix A.

**Table 1. Alternative approaches to calculating DALYs averted**

<table>
<tr><th></th><th></th><th>DALY 1</th><th>DALY 2</th><th>DALY 3</th><th>DALY 4</th></tr>
<tr><td>Survival effects (YLLs averted)</td><td></td><td>Based on indirectly estimating effects on survival from mortality (A)</td><td colspan="2">Directly estimated (D)</td><td rowspan="3">Directly estimated (G)</td></tr>
<tr><td rowspan="2">Morbidity Effects (YLDs averted)</td><td>Direct effect</td><td>Uses indirectly estimated effects on survival from mortality as a surrogate for morbidity effects (B)</td><td>Uses directly estimated survival effects as a surrogate for morbidity effects (E)</td><td rowspan="2">Directly estimated (F)</td></tr>
<tr><td>Indirect effect</td><td colspan="2">Uses average overall population health as a surrogate for increase in YLD burden associated with increase in YLLs averted (C)</td></tr>
</table>

***DALY 1***

The first estimate is based only on estimates of the mortality effects of changes in expenditure. As these are the most prevalent estimates available across the literature, this enables DALY 1 to be calculated using elasticities from various sources, such as the all-cause mortality elasticities that have been estimated in the UK as part of work on health opportunity costs (Claxton et al. 2017; Andrews et al. 2017).

The estimated elasticity for children under-5, $\in^{mortality}$, can be applied to the number of deaths observed in this age group in each province to provide an estimate of the number of deaths averted as a consequence of a 1% change in provincial health expenditure.

(1) $directly\ estimated\ deaths\ averted_i^{0-4} = 1\% * \left|\epsilon_{Canada}^{mortality^{0-4}}\right| * deaths_i^{0-4}$

Similarly, the estimated elasticities for male and female adults (ages 15-60) are applied to observed deaths by age and gender in each province, i.e., assuming that the proportionate effect on mortality applies equally across age groups within 15-60 age range.

(2) $directly\ estimated\ deaths\ averted_i^{15-60} = 1\% * \left|\epsilon_{Canada}^{mortality^{15-60}}\right| * deaths_i^{15-19} + \cdots + 1\% * \left|\epsilon_{Canada}^{mortality^{15-60}}\right| * deaths_i^{55-60}$

Once the likely deaths averted by a 1% change in health expenditure have been estimated in this way (see (1) and (2), the survival effects can be established by applying conditional life expectancy (CLE) at age of death to each death averted within each age group (see (3) and (4)). An estimate of survival gains of a change in health expenditure based on mortality effects (mortality based YLL averted) is simply the sum of these effects (5).

(3) $mortality\ based\ YLL\ averted_i^{0-4} = CLE_i^{0-4} * deaths\ averted_i^{0-4}$

(4) $mortality\ based\ YLL\ averted_i^{15-60} = CLE_i^{15-19} * deaths\ averted_i^{15-19} + CLE_i^{20-24} * deaths\ averted_i^{20-24} + \cdots + CLE_i^{55-59} * deaths\ averted_i^{55-59}$

(5) $mortality\ based\ YLL\ averted_i^{0-4\ \&\ 15-60} = mortality\ based\ YLL\ averted_i^{0-4} + mortality\ based\ YLL\ averted_i^{15-60}$

However, this measure (5) excludes potential survival effects in ages 5-14 years and also those over the age of 60. To try to reflect the possible survival effects across all ages the estimate of the YLL averted in (5) can be adjusted using the YLL in these age group as a proportion of the YLL across all ages, $\sigma_i$ (6),

(6) $mortality\ based\ YLL\ averted_i^{all\ ages} = \frac{mortality\ based\ YLL\ averted_i^{0-4\ \&\ 15-60}}{\sigma_i}$

where,

(7) $\sigma_i = \frac{YLL_i^{0-4} + YLL_i^{15-60}}{YLL_i^{all\ ages}}$

The YLL for each age group is simply the observed deaths in that age group multiplied by the conditional life expectancy for that age, i.e., it represents the survival burden of disease in each age and gender group. For example,

(8) $YLL_i^{0-4} = CLE_i^{0-4} * absolute\ deaths_i^{0-4}$

(9) $YLL_i^{15-60} = CLE_i^{15-19} * absolute\ deaths_i^{15-19} + CLE_i^{20-24} * absolute\ deaths_i^{20-24} + \cdots + CLE_i^{55-59} * absolute\ deaths_i^{55-59}$

The $YLL_i^{all\ ages}$ is calculated in a similar way to (8) and (9), as the sum of the product of absolute deaths and conditional life expectancy across all age groups in the population.

Therefore, the extrapolation of the survival effects from those age groups where mortality effects can be estimated (5) to all age groups in the population (6) assumes that the survival effects of changes expenditure are in proportion to the survival burden of disease at each age.

There are likely to be direct and indirect effects on morbidity of changes in expenditure. For example, changes in expenditure that affect mortality and survival are also likely to have an effect on morbidity through the prevention and treatment of disease (i.e., a direct effect decreasing YLD burden). However, an indirect effect may also be present as reductions in mortality and the resulting increased survival is likely to increase the number of years during which morbidity is experienced.

To calculate the possible direct effect we assume that the effect of changes in expenditure on morbidity is proportional to the effect on survival (B in Table 1), i.e., assuming that the estimated effects on the mortality burden of disease can be used as a surrogate for likely effects on morbidity burden where these effects have not been directly estimated. Since YLD data are not available by province, the ratio of YLD to YLL in Canada, $\gamma$, is applied to estimates of the province specific survival effects from (6) (see the first term of (12) below).

(10) $$\gamma = \frac{YLD_{CANADA}^{all\ ages}}{YLL_{CANADA}^{all\ ages}}$$

To account for the indirect effect of increasing the number of years during which morbidity is experienced due to the survival effects, we apply the per capita YLD burden for each province to the province specific survival effects (see the second term in (12) below and C in Table 1), Since province specific estimates of YLD are not available we assume that YLD are distributed across provinces in the same proportion as YLL (11), i.e., assuming that the morbidity burden of disease is likely to be higher (lower) where the survival burden is higher (lower).

(11) $$per\ capita\ YLD\ burden_i^{all\ ages} = \left(\frac{YLL_i^{all\ ages}}{YLL_{CANADA}^{all\ ages}} * YLD_{CANADA}^{all\ ages}\right) \Big/ population_i^{all\ ages}$$

Mortality based YLD averted are therefore calculated as:

(12)

$$mortality\ based\ YLD\ averted_i^{all\ ages} = mortality\ based\ YLL\ averted_i^{all\ ages} * \gamma - mortality\ based\ YLL\ averted_i^{all\ ages} * per\ capita\ YLD\ burden_i,$$

where the first term reflects the possible direct effects of expenditure in reducing morbidity (B in Table 1) and the second term captures the indirect effect of increases in morbidity due to increases in survival (C in Table 1).

The total DALYs averted due to a 1% change in health expenditure in each province is the sum of the survival effects (the YLL averted in (6), A in Table 1) and the net morbidity effects (YLD averted in (12), B-C in Table 1). This illustrates how estimates of mortality effects of health expenditure, in the form of elasticities, can be used to provide an indication of the likely survival (YLL averted) and morbidity effects (YLD averted). Although the elasticities applied to provincial data are for Canada as a whole, the health effects of a 1% change in provincial health expenditure will differ by province due to differences in the number observed deaths by age and gender and differences in age and gender specific conditional life expectancies. The amount of expenditure required to avert one DALY will also differ by province due to differences in total health expenditure.

(13) $$cost\ per\ DALY\ averted_i = \frac{1\% * government\ expenditure\ on\ health_i}{DALYs\ averted_i}$$

Nonetheless a number of assumptions have been required: i) that elasticities are similar across provinces; ii) that the estimates survival effects of changes in mortality are a good surrogate for morbidity effects; and iii) that the morbidity burden of disease is distributed across provinces in the same proportion as the survival burden of disease which can be calculated for each province.

***DALY 2***

The effect of changes in health expenditure on measures of survival burden of disease (YLL) can also be estimated directly from the cross country data (See Table 2). The estimated elasticity for YLL, $\epsilon^{YLL}$, is only available at a national rather than provincial level. However, assuming that elasticities are similar across provinces this elasticity can be applied to province specific $YLL_i^{all\ ages}$ which are calculated from observed mortality and conditional life expectancies by age and gender (e.g., see (8) and (9)) above). Therefore, YLLs averted due to a 1% change in health expenditure can be directly estimated (14) rather than applying conditional life expectancies to estimates of deaths averted by age and gender (as required in (1) to (7) above).

(14) $$directly\ estimated\ YLL\ averted = 1\% * \left|\epsilon_{Canada}^{YLL}\right| * YLL_i^{all\ ages}$$

The possible direct and indirect effects on morbidity of changes in health expenditure which effects survival can be calculated in the same way as previously; assuming that that the estimated effects on survival can be used as a surrogate for likely effects on morbidity and with the indirect effect of increases in morbidity based on directly estimated survival effects. Therefore, the net morbidity effects are calculated in the same way as in (12) but with *directly estimated YLL$_i$ averted* replacing *mortality based YLL$_i$ averted* (E-C in Table 1).

***DALY 3***

As well as direct estimates of the effect on survival burden of disease, the effect of changes in health expenditure on measures of morbidity burden of disease (YLD) can also be estimated directly from the cross country data (See Table 2). DALY 3 uses direct estimates of the effect on survival burden in the same way as DALY 2 but combines these with direct estimates of the effect on morbidity. The estimated elasticity for YLD is only available at a national rather than provincial level. However, assuming that elasticities are similar across provinces this elasticity can be applied to province specific estimates of morbidity burden. Since province specific estimates of YLD are not available we assume that YLD are distributed across provinces in the same proportion as YLL as previously (11). The directly estimated YLD averted for a 1% change in provincial health expenditure is simply the product of the estimated YLD for that province and the estimated YLD elasticity for Canada (15).

(15) $$directly\ estimated\ YLD\ averted = 1\% * \left|\epsilon_{Canada}^{YLD}\right| * YLD_i^{all\ ages}$$

The total DALYs averted due to a 1% change in health expenditure in each province is the sum of the directly estimated survival effects (YLL averted in (14), D in Table 1) and the directly estimated morbidity effects (YLD averted in (15), F in Table 1).

***DALY 4***

The combined effect of changes in expenditure on survival and morbidity burden of disease (DALYs can also be estimated directly from the cross country data using country level estimates of DALY burden of disease (See Table 2). As for mortality, YLL and YLD the estimated elasticity for DALYs is only available at a national rather than provincial level but can be applied to province specific estimates of DALY burden assuming that the estimated elasticity is similar across provinces. Since province specific estimates of DALY burden are not available we assume, similar to previously, that DALY burden of disease is distributed across provinces in the same proportion as the survival burden of disease which can be calculated for each province (see (6), (7) and (11)). Therefore, a direct

estimate of DALYs averted for a 1% change in provincial health expenditure is simply the product of the estimated DALY burden for that province and the estimated elasticity for Canada (16).

(16) $$directly\ estimated\ DALY\ averted = 1\% * \left|\epsilon_{Canada}^{DALY}\right| * DALY_i^{all\ ages}$$

These 4 alternative ways to estimate health opportunity costs, as measured by the cost per DALY averted, make slightly different assumptions. One common one is that estimated elasticities, which are currently only available at a national level, can be applied equally across provinces. This might not be unreasonable since the differences in elasticities between countries are quite small based on Bokhari et al (2007), although this model only allows for two interaction terms which both have modest effects. The other common assumption is that the morbidity burden of disease, which is currently not available by province, is distributed across provinces in the same way measures of survival burden ($YLL_i$) which can be calculated at a provincial level. This might be reasonable for larger provinces which have similar epidemiology, but is less likely to be reasonable for smaller provinces which differ in the distribution of types of disease and its impact.

Nonetheless, the comparison of DALY 1 with DALY 4 does give some indication of whether it is reasonable to use estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects. This is particularly useful as other studies in high income countries have estimated elasticities for mortality outcomes using high quality within country data which overcomes some of the difficulties and challenges of estimation based on aggregate country level data. As a sensitivity analysis we apply two different all-cause mortality elasticities estimated for the UK (Claxton et al 2017 and Andrews et al 2017) in place of the mortality elasticities based on Bokhari et al to re-calculate cost per DALY averted for DALY 1.

## 3. Results

### *Estimated elasticities for Canada*

The extended Bokhari et al. (2007) model generated country-specific elasticities for all of the countries in the model (n=127). Elasticities only differed between countries due interactions with level of infrastructure and shocks in donor funding. The elasticities for Canada for each of the six measures of health outcome are reported in Table 2 along with the average elasticities of all 25 high income countries (HICs) in the dataset.[1]

[1] Countries included: Australia, Austria, Canada, Chile, Croatia, Estonia, Finland, France, Germany, Hungary, Italy, Japan, Lithuania, Netherlands, New Zealand, Portugal, Singapore, South Korea, Spain, Sweden, Switzerland, Trinidad and Tobago, United Kingdom, United States and Uruguay. St Kitts and Nevis is also excluded for the sake of comparison across outcomes due to its missing outcome data for DALY, YLL and YLD models.

**Table 2. Estimated elasticities for Canada**

| Mortality (deaths per 1,000) | Canada | Average for high income countries |
|---|---|---|
| Children under-5 | -0.3412 | -0.3549 |
| Adults females | -0.1924 | -0.1944 |
| Adult males | -0.1928 | -0.2000 |
| DALYs | -0.2137 | -0.1929 |
| YLLs | -0.3032 | -0.2765 |
| YLDs | -0.0294 | -0.0246 |

The elasticities for Canada are comparable to the mean of estimates for other HICs. Among HICs very few receive donor funding, which means that the primary driver of differences in estimated elasticities is due to the interaction term combining spending and level of infrastructure (proxied by 'paved roads per unit of area'). Canada has a very low value for this variable, due to the sparsity of its population, and so this is almost entirely responsible for why there are small differences between Canada's estimated elasticities and the average for all HICs.

***Cost per DALY averted***

The estimates of cost per DALY averted for Canada as a whole and for each province are reported in Table 3 and are also expressed as a % of provincial GDP per capita.

The estimates of cost per DALY for Canada as a whole are not the average of the cost per DALY ratios across the provinces but the ratio of the sum of changes in expenditure to the sum of DALYs averted across the provinces. The cost per DALY for Canada as a whole is similar using DALY 1 and DALY 4 which does give some indication that it might be reasonable to use estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects. This is also reflected in the results by province where DALY 1 and DALY 4 tend to provide relatively similar estimates, with the exception of two provinces (Prince Edward Island and Yukon).

DALY 2 consistently provides the lowest cost per DALY for Canada as a whole and across the provinces. This reflects the fact that the estimated elasticity for survival effects (YLL) is greater in magnitude than for adult mortality (see Table 2). This larger, directly estimated, effect on survival (YLL averted) is then used as a surrogate for morbidity effects. However, DALY 3 consistently provides the highest cost per DALY estimate for Canada and for each of the provinces. This reflects fewer DALYs averted due to the much lower magnitude of the estimated elasticity for morbidity effects (YLD, see Table 3), i.e., the smaller effect on morbidity more than offsets the larger effect on survival compared to DALY 1 (with the exception of Yukon). Although these differences and the differences in the elasticities reported in Table 2 might indicate that mortality effects underestimate survival effects in adult populations and that both mortality and survival effects may overestimate morbidity effects, this should not be over-interpreted as the estimated elasticities are not based on Canadian within country data but country level data with limited interactions for country level effects. However, in general the comparison of DALY 1 and DALY 4 does suggest that using estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects may not be unreasonable albeit with additional uncertainty.

**Table 3. Cost per DALY averted and as a percent of GDP per capita by province**

| | Cost per DALY averted (2013 C$) | | | |
|---|---|---|---|---|
| | DALY 1 | DALY 2 | DALY 3 | DALY 4 |
| Canada | $97,321 | $66,661 | $113,681 | $89,334 |
| | 180% | 123% | 211% | 165% |
| Alberta | $125,997 | $87,175 | $149,636 | $117,589 |
| | 147% | 102% | 175% | 137% |
| British Columbia | $96,042 | $64,335 | $109,752 | $86,247 |
| | 193% | 129% | 220% | 173% |
| Manitoba | $104,498 | $72,502 | $122,729 | $96,444 |
| | 212% | 147% | 249% | 196% |
| New Brunswick | $90,166 | $60,247 | $101,819 | $80,013 |
| | 214% | 143% | 242% | 190% |
| Newfoundland and Labrador | $104,902 | $70,603 | $119,022 | $93,531 |
| | 161% | 108% | 182% | 143% |
| Northwest Territories | $249,536 | $175,519 | $298,690 | $234,720 |
| | 248% | 175% | 297% | 234% |
| Nova Scotia | $89,814 | $60,108 | $101,360 | $79,652 |
| | 219% | 147% | 248% | 195% |
| Nunavut | $177,375 | $142,492 | $236,380 | $185,755 |
| | 282% | 226% | 376% | 295% |
| Ontario | $95,706 | $65,573 | $112,111 | $88,101 |
| | 187% | 128% | 219% | 172% |
| Prince Edward Island | $82,939 | $54,791 | $91,618 | $71,997 |
| | 212% | 140% | 234% | 184% |
| Quebec | $87,446 | $60,013 | $102,159 | $80,280 |
| | 196% | 134% | 228% | 180% |
| Saskatchewan | $99,467 | $69,497 | $117,491 | $92,328 |
| | 132% | 92% | 156% | 123% |
| Yukon | $155,899 | $102,780 | $173,830 | $136,601 |
| | 217% | 143% | 242% | 190% |

The four alternative ways to calculate cost per DALY averted provide quite similar estimates across most provinces. To some extent this might be expected as it is assumed that estimated elasticities, which are currently only available at a national level, can be applied equally across provinces. Insofar as provinces have similar health expenditure per capita and similar mortality rates, conditional life expectancies and population distribution, the cost per DALY averted will inevitably be very similar. This also explains why the cost per DALY averted differs for some of the smaller provinces where per capital heath expenditure is higher and where the population, mortality rates and conditional life expectancies differ from the larger provinces (e.g., Yukon, Northwest Territories and Nunavut).

Figure 1 illustrates the range of estimates for Canada and for each province by under-5 mortality rate. The average of the range of values for each province is not the average for the four cost per DALY ratios but the ratio of a 1% change in expenditure to the average DALYs averted across these

four estimates. Few strong patterns emerge but it is clear that the epidemiology of Nunavut and to some extent Northwest Territories is quite different to the other provinces. The high under-5 mortality in Nunavut would, other things equal tend to reduce the cost per DALY averted. However, this is more than offset by the higher per capita health expenditure and lower conditional life expectancies.

**Figure 1. Cost per DALY averted by under-5 mortality rate**

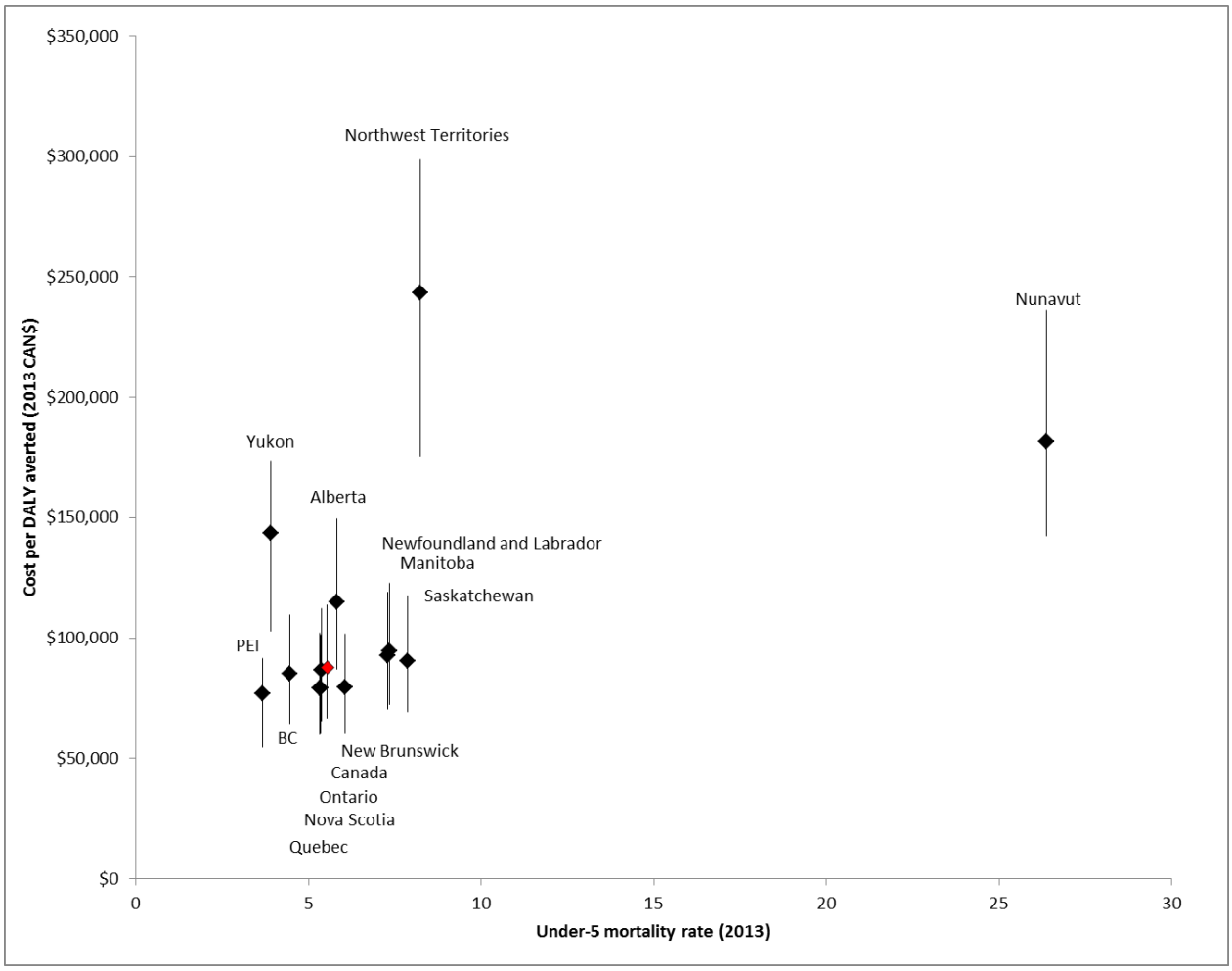
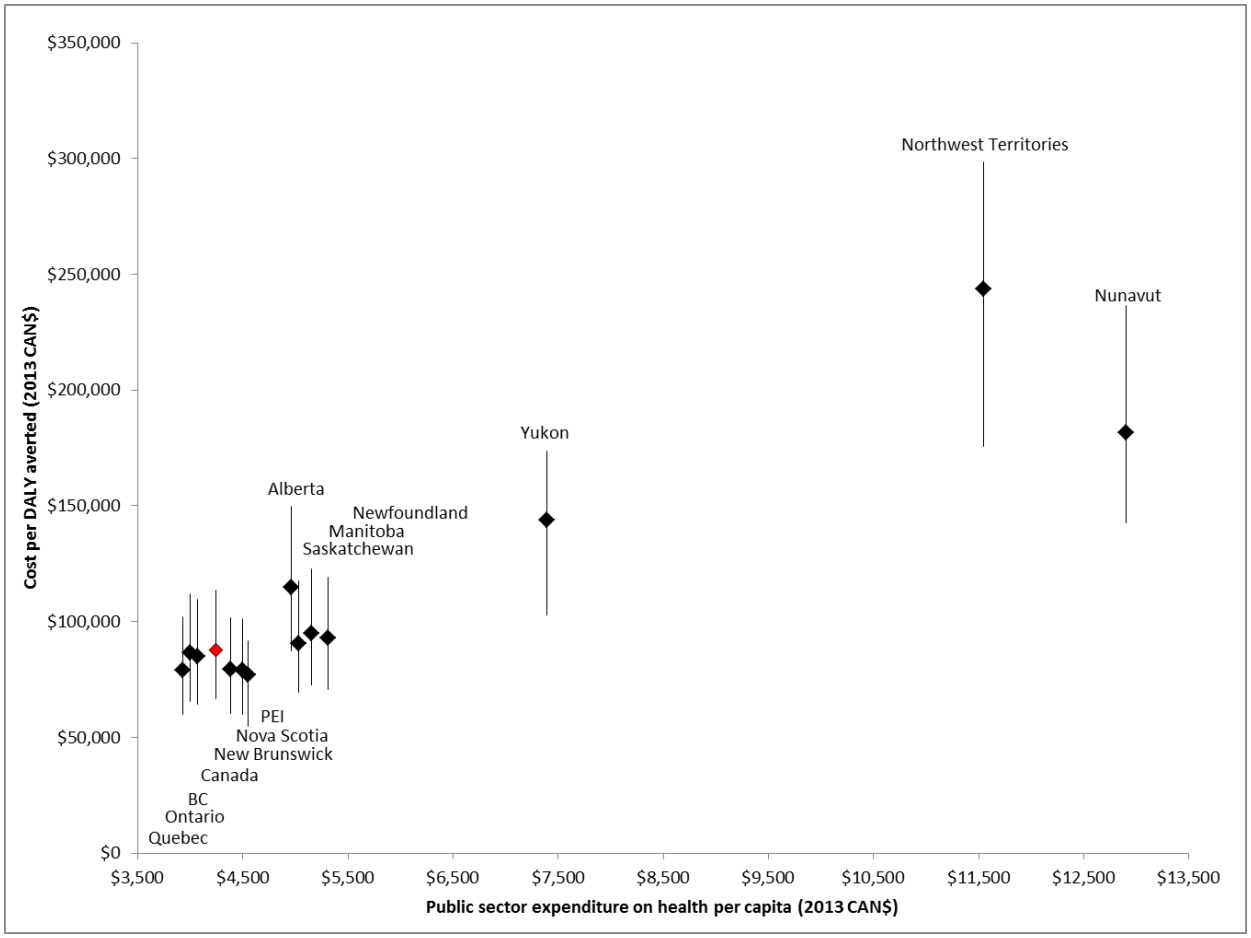



Figure 2 illustrates the same cost per DALY averted estimates but now by per capita public expenditure on health. It suggests that the cost per DALY averted increases with per capita health expenditure which is, in general, what might be expected, although this is to some extent inevitable given the methods used to generate these estimates. It also illustrates the similarity in the range of estimates for most provinces but also why others (Yukon, Northwest Territories and Nunavut) differ. The apparent similarity in the range of cost per DALY averted between most provinces should not be over interpreted as estimates would also be expected to differ if provinces are able to generate health at different rates, which would be reflected in differing elasticities. This underscores the importance of further research to estimate these values at the provincial level in Canada using within country and within province data.

**Figure 2. Cost per DALY averted by per capita public expenditure on health**




***Sensitivity analysis***

Table 4 reports the cost per DALY averted (DALY 1) for Canada and by province using all-cause mortality elasticities from Claxton et al. (2017) and Andrews et al. (2017), which are applied equally to under-5 and adult mortality. Claxton et al (2017) estimated mortality elasticities by disease area, which were combined with mortality data to produce an implied all-cause mortality elasticity estimate of -1.0278 for 2012/13 expenditure data and 2012/13 to 2014/15 mortality data. Andrews et al (2017) used an alternative approach to identification but applied it to total expenditure and mortality outcomes to directly estimate an all-cause mortality elasticity of -0.705 for 2005/06. The important differences between Claxton et al (2017) and Andrews et al (2017) are the year of analysis, the approach to identification and the level of aggregation. Recent work reported in Claxton et al (2017) does not suggest strong trends in implied all cause elasticities over the previous 10 years of expenditure data, i.e., assuming elasticities to be stable over time is not unreasonable. On-going work also suggests that the two approaches to identification (when applied at disease area level) generate similar cost per QALY estimates for the UK.

Although differences in estimated elasticities and cost per QALY based on these approaches are not statistically significant, in general direct estimates of all cause elasticities tend to be lower than those implied by estimates at disease area level. This is to be expected as all cause estimates will be subject to some aggregation bias compared to those which are able to capture any heterogeneity of effect by disease area. Both estimates are higher in magnitude than the mortality elasticity

estimates from the extended Bokhari et al (2007) model. Again, this might be expected given the greater dangers of aggregation bias using country level data and the difficulty of fully accounting for unobserved heterogeneity and endogeneity using the instruments for health expenditure that are available across countries. These differences in estimated all cause elasticities are reflected in the cost per DALY averted with the lowest associated with Claxton et al (2017) and the highest with Bokhari et al (2007).

**Table 4. Cost per DALY averted based on alternative estimates of mortality effects**

| | Cost per DALY averted for DALY 1 (2013 C$) | | |
|---|---|---|---|
| | Claxton et al (2017) | Andrews et al (2017) | Bokhari et al (2007) |
| Canada | $19,914 | $29,032 | $97,321 |
| Alberta | $26,060 | $37,991 | $125,997 |
| British Columbia | $19,227 | $28,029 | $96,042 |
| Manitoba | $21,722 | $31,667 | $104,498 |
| New Brunswick | $18,265 | $26,628 | $90,166 |
| Newfoundland and Labrador | $21,392 | $31,186 | $104,902 |
| Northwest Territories | $52,191 | $76,087 | $249,536 |
| Nova Scotia | $18,002 | $26,244 | $89,814 |
| Nunavut | $41,776 | $60,903 | $177,375 |
| Ontario | $19,606 | $28,582 | $95,706 |
| Prince Edward Island | $16,425 | $23,945 | $82,939 |
| Quebec | $17,936 | $26,147 | $87,446 |
| Saskatchewan | $20,804 | $30,329 | $99,467 |
| Yukon | $30,633 | $44,659 | $155,899 |

Setting aside the three provinces which have especially high per capita public health expenditure (Yukon, Northwest Territories and Nunavut) the range of potential cost per DALY averted for Canada and for the other provinces is in the region of $20,000 to $100,000 per DALY averted. The lower part of this range is consistent with the implied cost per QALY gained for Canada based on the analysis in Woods et al 2016 ($25,292 to $31,915 in 2013 US$). The relatively modest difference between the remaining provinces follows the same pattern as seen previously in Table 3 and Figure 1 and 2. However, as discussed above, these apparent similarities should not be over-interpreted as the estimated elasticities are applied equally across provinces. Insofar as provinces have similar health expenditure per capita and similar mortality rates, conditional life expectancies and population distribution, then the cost per DALY averted will inevitably be very similar. These considerations and the wide range of potential estimates of cost per DALY averted using currently available estimates in Table 4 indicates the importance of further research to provide province specific elasticity estimates for Canada using within country and within province data.

## 4. Discussion

Estimates of the health opportunity costs of additional health care expenditure are critical for informing assessments of whether the improvement in health outcomes offered by investing additional resources in a new health technology exceeds the improvement in health that would have been possible if the additional resources required had, instead, been made available for other health care activities. Commonly established implied norms, such as 1-3x GDP per capita, are often inappropriately applied in practice to judge cost-effectiveness (Bertram et al. 2016). Such values generally reflect the social demand for health (i.e., a view of what value ought to be placed on improvements in health) rather than an evidence based assessment of health opportunity costs given actual levels of expenditure. As such, they do not reflect the health that the HCS is currently able to deliver with the resources available, i.e., the 'supply side' of the HCS. Adopting 'thresholds' to judge costs effectiveness which are too high and do not reflect the 'supply side' will lead to decisions that reduce overall health because the health gained from adopting a new technology will be more than offset by the health opportunity costs elsewhere in the HCS. It will also mean that the HCS will pay too much for the benefits offered by new branded pharmaceuticals because the additional cost of patented innovations will do more harm than good for population health during the remaining patent period. As well as leading to net harms for population health it may also exacerbate health inequalities and unwarranted variations in access to other health care, depending on where the health opportunity costs of additional health care costs tend to fall.

The framework of analysis set out in this report illustrates how estimates of the relationship between mortality and variations in health care expenditure can be employed alongside province specific data on demography, epidemiologic profile and expenditure to inform estimates of health opportunity costs. While data is readily available for the latter, reliable estimates of the relationship between mortality and variations in health care expenditure present a challenge.

This report employed estimates estimated using the model used by Bokhari et al (2007), which applies an instrumental variable method to cross-sectional data, and models both public expenditure on health and a country's GDP as endogenous variables. While Bokhari et al. (2007) find a statistically and economically significant effect of public expenditure on health reducing mortality outcomes, there is no clear and consistent finding in the literature that evaluates the relationship between mortality and variations in health care expenditure using country level data (Gallet & Doucouliagos 2017). This is often driven by the methodological approach adopted by each study, addressing the considerable challenges including the important country-level heterogeneity, much of which is unobserved and controlled for using existing data, even if it is assumed that systematically unbiased measurements are available. Estimates of mortality elasticities based on country level data tend to be lower than those based on within country data which are likely to reflect the greater dangers of aggregation bias using country level data and the difficulty of fully accounting for unobserved heterogeneity and endogeneity using the instruments for health expenditure that are available across countries.

The framework of analysis employed here can be applied to the results of any econometric study which is thought to identify plausible effects on mortality of changes or differences in health expenditure. Other within-country studies have estimated the marginal productivity of health expenditure in producing health (QALYs) (Martin et al. 2008; Claxton, Martin, et al. 2015; Edney et

al. 2017; Vallejo-Torres et al. 2016). A sensitivity analysis was conducted based on recent work in the UK, where all-cause mortality elasticity estimates have been estimated using an instrumental variable approach with different devolved health care bodies as the unit of observation providing the variation in expenditures, outcomes and health care need variables. The implied all-cause mortality elasticity estimate, -1.0278, found by Claxton et al (2017) is considerably higher in magnitude to any of the mortality elasticity estimates from the extended Bokhari et al (2007) model. Another study, Andrews et al (2017) used an alternative approach to identification to directly estimate an all-cause mortality elasticity estimate for the UK NHS of -0.705. Once again, this is higher than the results from Bokhari et al (2007). Using these two elasticities (-1.0278 and -0.705) as inputs for the calculation of the DALYs averted from a 1% change in expenditure results in a considerably lower estimates of the cost per DALY averted for Canada ($19,914 and $29,032 respectively) and for the provinces (see Table 4).

These estimates are from within-country studies of the relationship between health and expenditures, set in the context of the UK, which form part of a growing literature of studies of this kind. Edney et al (2017) and Vallejo-Torres et al (2016) perform similar studies in the contexts of Australia and Spain. The overall results in terms of expenditure per QALY give similar results to these UK studies, but the elasticities cannot be directly compared. In the case of Edney et al. (2017), an elasticity, -1.602, is estimated on HRQoL-weighted YLL reflecting the percentage change in QALYs resulting from delayed mortality for a given percentage increase in expenditure. Vallejo-Torres et al. (2016) instead estimate an elasticity, -0.0681, reflecting the percentage effect on Quality Adjusted Life Expectancy (QALE) that results from a given percentage increase in expenditure in a given year, which would then need to be sustained over the lifetime period (Lichtenberg 2004).

Previous work has estimated cost per DALY averted for 123 low- and middle-income countries based on elasticities estimated from the Bokhari et al (2007) model but using country level data on health expenditure, epidemiology and demographics from the Global Burden of Disease database and the World Bank (Ochalek et al. 2015). Using these sources, which have been standardised to be internationally comparable, rather than Canadian data would have resulted in slightly higher estimates of the DALYs averted from health expenditure so slightly lower cost per DALY averted estimates ($53,048 to $89,827 per DALY averted rather than $66,661 to $113,681 using Canadian data in Table 3). However, it is the larger differences due to alternative but plausible effects on mortality of changes in health expenditure illustrated in Table 4 which indicate the importance of further research to provide province specific elasticity estimates for Canada using within country and within province data.

## 5. Recommendations

The range of potential cost per DALY averted for Canada and for most provinces is in the region of $20,000 to $100,000 per DALY averted in Table 4, with the lower estimates associated with more recent work using within country rather than country level data. Given the greater dangers of aggregation bias of using country level data and the difficulty of fully accounting for unobserved heterogeneity and endogeneity using the instruments for health expenditure that are available across countries, it is the lower end of this range that might be regarded as more plausible. An assessment that elasticities using within country data for Canada are likely to be higher than those based on country level data is plausible and tends to be supported by growing literature from other countries.

***A cost per DALY threshold is likely to be less than $50,000 for Canada as a whole and is likely to be similar across most provinces.***

A measure of heath benefit more appropriate to Canada would be QALY gained rather than DALYs averted. However, currently there are no estimates of QALY burden of disease which would allow estimates of the mortality effects of changes in expenditure to be used to estimate a cost per QALY threshold.

Nonetheless, estimates of cost per DALY averted and costs per QALY gained of changes in expenditure are likely to be similar. Although there will be important differences between the same effects measured as QALYs gained or DALYs averted in particular diseases (due to differences in health state descriptions and weights attached to disability and quality of life) (Robberstad 2009), these are not systematic so DALY and QALY effects on average across all disease areas are unlikely to differ markedly. Importantly the type of age related weights previously used in calculating DALYs, which would lead to more systematic differences have not been used. However, one aspect of how DALYs averted are calculated does suggest that (other things equal) DALYs averted will then to underestimate QALY gains. This because reductions in mortality and increases in survival changes conditional life expectancies so increases the burden of disease as measured by DALYs (Airoldi & Morton 2009).

***A cost per QALY threshold is likely to be similar or lower than a cost per DALY averted threshold***

This is also consistent with the range of implied cost per QALY gained for Canada based on the analysis in Woods et al 2016 ($26,596 - 33,560 in 2013 CAN), which extrapolates the UK findings based on estimates of the income elasticity of demand for health and assumptions about the relative underfunding of HCS (i.e., the shadow price for public expenditure on health). Estimates based on this analysis have been adopted in Norway while further research using within country data are explored. Using the approach taken by Norway (assuming and income elasticity of one) would provide a cost per QALY threshold for Canada of $28,089.

***A cost per QALY threshold of $30,000 per QALY would be a reasonable assessment of the health effects of changes in health expenditure for Canada as a whole and is likely to be similar across most provinces.***

The currently available estimates of the effect of changes in health expenditure on mortality outcomes have focused on the effects of changes in public rather than private expenditure. The

estimates for Canada applied these estimated elasticities to public expenditure (federal and provincial). Applying the same elasticities to total expenditure (including private expenditure) would not change the estimates of cost per DALY averted. However, if estimated elasticities of public and private expenditure differ, then the cost per QALY gained or cost per DALY averted of changes in public and private expenditure would also differ, e.g., if the marginal productivity of private expenditure is lower than public expenditure the cost per QALY threshold for changes in private expenditure will be higher. However, in the absence of evidence of differences in the marginal productivity of public and private health expenditure adopting the same cost per QALY threshold for both categories of expenditure would not be unreasonable. Adopting a threshold to that reflects health opportunity costs of public health expenditure will ensure that prices of new pharmaceuticals do not undermine health outcomes of publically funded health care.

## 6. Further research

Further research to provide Canadian and/or province specific elasticity estimates using within country and within province data should be regarded as a priority. Improving estimates of health opportunity costs for the Canadian provinces could focus on the following issues: i) estimating mortality elasticities for Canada as a whole or for each of the provinces using within country data; ii) developing estimates of QALY rather than DALY burden of disease that are province specific and iii) directly estimating the effect of changes in health expenditure on QALY outcomes for each province.

### *Estimating mortality elasticities for Canada using within country data*

Estimates of an all cause mortality elasticity for Canada as a whole could exploit cross sectional variation in expenditure and outcomes, seeking potential instruments from socioeconomic variables and/or exogenous elements in how funding tends to be allocated, following Claxton et al (2017) and Andrews et al (2017) respectively. This would start to identify where in the $20,000 to $100,000 range might be most plausible. However, it would still require that a single elasticity estimated at a national level be applied equally across all provinces. It would also mean that differences between provinces would be modest and may not reflect real differences in the marginal productivity for health care expenditure, i.e., insofar as provinces have similar health expenditure per capita and similar mortality rates, conditional life expectancies and population distribution, then the cost per DALY or QALY estimates will also be very similar. This could be relaxed by attempting to estimate all cause elasticities for each province. This might be possible using interaction terms for province when estimating a national all cause model or estimating separate province specific all cause models. The latter poses the challenge of finding units of analysis with sufficient variation in expenditure and outcomes within province as well as suitable instruments.

However, in general, direct estimates of all cause elasticities tend to be lower than those implied by estimates at disease area level because they are likely to be subject to some aggregation bias compared to those which are able to capture any heterogeneity of effect by disease area. Therefore, it would be an advantage to estimate elasticities (national and provincial) by disease areas. However this would require expenditure by disease area as well as mortality outcomes to be available at the unit of analysis that will provide sufficient variation. Nonetheless estimates of all cause elasticities for Canada and/or the provinces based on within country data would be a

significant improvement over existing estimates, whether or not they are directly estimated or implied by estimates at disease area level.

***Province specific estimates of QALY burden of disease***

The analysis above applies estimated all cause elasticities to measures of burden of disease by province. The survival burden of disease is province specific; using data on deaths by age and gender and conditional life expectancies for each province. However, measures of morbidity burden of disease are not routinely available, so a measures of morbidity for Canada as a whole have been used (YLD) from the Global Burden of Disease data base. This poses two difficulties. Province specific estimates of YLD are not available so it is assumed that YLD are distributed across provinces in the same way as survival burden ($YLL_i$) i.e., assuming that the morbidity burden of disease is likely to be higher (lower) where the survival burden is higher (lower). The second problem is that the measure of health effect of changes in expenditure is expressed using the measures of disease burden that are currently available, i.e., DALY averted (DALY = YLL+YLD) rather than QALYs, which would be more appropriate to decision making processes in Canada because it is more likely to reflect the dimensions of quality of life and preferences for health states relevant to Canada (Airoldi & Morton 2009; Robberstad 2009).

The QALY effects of changes in expenditure could be estimated from mortality elasticities based on measures of the QALY burden of disease across provinces. This would require age and gender quality of life norms and decrements in quality of life due to disease. It would also require estimates of the incidence and duration of disease, as well as mortality and conditional life expectancies. This was the approach taken in the UK which estimated QALY burden of disease for all 3 digit ICD codes (Claxton et al 2015). However, this work estimated elasticities by disease area which were then applied to QALY burden in each disease area rather than applying an all cause elasticity to a measure of the total QALY burden of disease.

***Estimating the effect of changes in health expenditure on QALY outcomes for each province***

Measures of QALY burden of disease for each province would overcome some difficulties and allow results to be expressed as cost per QALY gained rather than DALY averted. However, such cost per QALY estimates would still require an assumption that estimates of the mortality effects of changes in expenditure are a good surrogate for a more complete measure of the health effects which include survival and quality of life.

The similarities between estimates based on DALY 1 and DALY 4 for Canada as a whole and for most provinces in Table 3 does give some indication that it might be reasonable to use estimates of the mortality effect of changes in health expenditure as a surrogate for likely survival and morbidity effects. Estimates in the UK are founded on similar assumptions since quality of life outcomes by disease and geographic areas are not available to directly estimate them. More recently these assumptions have been examined by conducting a formal quantitative elicitation exercise with UK clinical experts in the key disease areas. The results of this expert elicitation suggest that the assumptions required are not unreasonable and, if anything, are likely to underestimate the effects of changes in health expenditure in the UK (Soares et al. 2018).

Therefore, Canada could rely on similar assumptions and focus efforts on estimating mortality based elasticities, ideally by province, if possible by disease area, combined with measures of QALY rather than DALY burden of disease. A similar approach to elicitation could be conducted with clinical experts from Canada focusing on key disease areas relevant to each province. Alternatively, attempts could be made to directly estimate the effects of changes in expenditure on quality of life outcomes. There are no examples of where that has been done by disease area, but other studies have been able to estimate the effect on mortality and survival separately from effect on quality of life outcomes (Edney et al. 2017) or directly estimate the effect on changes in quality adjusted life expectancy, which in principle captures both effects (Vallejo-Torres et al. 2016). Direct estimation of QALY effects by province would be ambitious and would require careful consideration of whether the type of quality of life data, at the unit of observation available, would offer sufficient variation. Although the combination of cross sectional and time series data does offer more opportunities for estimation, the high persistence often found in these data, especially in the UK, may mean that it is variation in the cross sectional data that is likely to be most important.

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**Appendix A. Variables used to calculate DALYs averted**

| Variable | Measure used | Source | Year used |
|---|---|---|---|
| 1-year probability of death for females, males and both for ages in a given five-year age category (n-n+4) | Where life table data is given by 1-year age group:<br>$P(annual\ mortality\ n\ to\ n+4) = 1 - \left(\prod_{t=n}^{n+4}(1-p_t)\right)^{\frac{1}{5}}$<br>Where life table data is given by 5-year age group:<br>$P(annual\ mortality\ n\ to\ n+4) = 1 - (1-p_{n\ to\ n+4})^{\frac{1}{5}}$ | Statistics Canada. 2017. Life tables, Canada, provinces and territories, catalogue no. 84-537-X. http://www.statcan.gc.ca/pub/84-537-x/84-537-x2017001-eng.htm | 2011-2013 |
| Absolute number of death for females, males and by five-year age category (n-n+4) | $Absolute\ deaths\ n\ to\ n+4 = P(annual\ mortality\ n\ to\ n+4) * population\ n\ to\ n+4$ | Calculated variables from life tables. | |
| Conditional life expectancy for females, males and both by five-year age category (n-n+4) | $e_x$ by 5-year age category 0-90+.<br>Where $e_x$ given by year $e_x$ for lowest age in category used.<br>Where $e_x$ given for over 90 $e_x$ at 90 used. | Statistics Canada. 2017. Life tables, Canada, provinces and territories, catalogue no. 84-537-X. http://www.statcan.gc.ca/pub/84-537-x/84-537-x2017001-eng.htm<br>$e_x$ given by year (0-110+) for all provinces except Prince Edward Island, Nunavut, Northwest Territories and Yukon. | |
| Population by females, males and both by five-year age category (n-n+4) | Population by 5-year age category 0-100+. | Statistics Canada. Table 051-0001 - Estimates of population, by 5-year age group 0-100+) and sex for July 1, Canada, provinces and territories, annual (persons unless otherwise). CANSIM: http://www5.statcan.gc.ca/cansim/a26?id=510001 | 2013 |

| | | | |
|---|---|---|---|
| Per capita GDP expenditure based at current prices ($' 000) | GDP expenditure based / Total Population | GDP: Statistics Canada, CANSIM, table 384-0038.<br><br>Total Population: Statistics Canada, CANSIM, table 051-0001. | 2013 |
| Public sector expenditure on health (provincial government; federal direct; municipal government; social security funds) | Total value, current dollars | National Health Expenditure Database, 1975 to 2016, Canadian Institute for Health Information.<br>Excel Sheet: nhex-Series-D3-2016_en.xlsx<br>https://www.cihi.ca/en/national-health-expenditure-trends | 2013 |

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# Regulations Amending the Patented Medicines Regulations

**Statutory authority**

*Patent Act*

**Sponsoring department**

Department of Health

## REGULATORY IMPACT ANALYSIS STATEMENT

(*This statement is not part of the Regulations.*)

### Executive summary

**Issues:** The Patented Medicine Prices Review Board (“PMPRB” or “the Board”) uses a regulatory framework that currently falls short of its mandate to protect Canadian consumers from excessive prices for patented medicines. Canada’s patented medicine prices are among the highest in the world, and despite significant changes in the medicine market, the *Patented Medicines Regulations* have not been substantively changed in over two decades. The Regulations need to be modernized to provide the PMPRB with more relevant and effective regulatory tools in order to better protect Canadians from excessive prices for patented medicines.

**Description:** This proposal would amend the *Patented Medicines Regulations* (“Regulations”) so that the PMPRB’s regulatory framework includes new price regulatory factors and patentee price information reporting requirements that will help the PMPRB to protect Canadian consumers from excessive prices. There are five elements.

*New price regulatory factors and updating the schedule of comparator countries*

(1) Providing the PMPRB with three new price regulatory factors to enable it to consider the price of a patented medicine in relation to its value to patients and impact on the health care system.

(2) Updating the schedule to the Regulations that sets out the countries (now the PMPRB7) on which patentees report pricing information to include countries with similar consumer protection priorities, economic wealth, and marketed medicines as Canada. This would provide the PMPRB with the information needed to regulate prices based on comparisons that are more closely aligned with the PMPRB's mandate and Canada's domestic policy priorities.

*New reporting requirements*

(3) Reducing reporting obligations for patented veterinary, over-the-counter and "generic" medicines (i.e. those authorized for sale by the Minister of Health through an Abbreviated New Drug Submission [ANDS]). As these products pose a lower risk of asserting market power and charging excessive prices, this reduction would enable the PMPRB to focus on medicines at higher risk of excessive pricing.

(4) Amending patentee price information reporting requirements to include reporting in relation to the new factors.

(5) Requiring patentees to report price and revenue information net of all price adjustments such as direct or indirect third party discounts or rebates. This would ensure that the PMPRB is fully informed of the actual prices for patented medicines in Canada and enhance the relevance and impact of domestic price comparisons.

**Cost-benefit statement:** The proposed amendments would produce an estimated net benefit to Canadians of $12.6 billion net present value (NPV) over 10 years due to reduced prices for patented medicines. Lower prices would alleviate financial pressures on public and private insurers and improve affordable access for Canadians paying out-of-pocket. Lost revenues to industry are estimated to be $8.6 billion present value over 10 years. Costs to industry are estimated to be $9K/year in total, including administrative and compliance costs. Government costs of approximately $8.8M/year (PV) would include increasing the PMPRB's staff and resources for an anticipated increase in compliance and enforcement activities.

It is not anticipated that these amendments would generate adverse impacts on industry employment or investment in the Canadian economy. Although when the current regulatory framework was first conceived 30 years ago, policy makers believed that patent protection and price were key drivers of medicine research and development (R&D) investment, there is no evidence of this link. The level of industry R&D investment relative to sales by medicine patentees in Canada has been falling since the late 1990s and is now at a historic low despite Canada having among the highest patented medicine prices in the world. These amendments would aim to align Canadian prices with those in countries that, despite having lower prices, receive higher medicine industry investment.

**"One-for-One" Rule and small business lens:** The "One-for-One" Rule applies and the anticipated administrative burden is estimated to be $3,062 (2012 dollars) annually. The small business lens does not apply.

**Domestic and international coordination and cooperation:** Price regulations on medicines are a common international practice, although there is a significant variation in approach. These differences often arise from a need to tailor policy instruments to work within each

country's health care system. While countries monitor foreign models, it is to keep abreast of international best practices, rather than to harmonize. Regulating the prices for patented medicines to be non-excessive is not subject to trade provisions.

## Background

*Patented medicines are an important part of Canada's health care system*

Patented medicines help prevent and cure disease as well as save lives. But Canadians are not getting the value for money on prescription medicine spending or the outcomes they deserve. Medicine spending in Canada has increased from less than 10% of total health expenditure, when Medicare was first established 49 years ago, to about 16% today. Medicines are now the second-largest category of spending in health care, ahead of physician services and behind total hospital spending (which includes medicines used in hospital). Canadians are spending more per capita on medicines than any other country in the world, with the exception of the United States. Greater medicine expenditures can limit access to innovative medicines by straining the budget envelope for medicines of public and private insurers, place a financial burden on patients who pay out of pocket for their medicines, and mean fewer resources for other critical areas of the health care system.

In January 2016, federal, provincial and territorial ministers agreed to work together to improve the accessibility, affordability, and appropriate use of medicines to better meet health care system needs. The Government of Canada is committed to this work and is taking action to lower the cost of medicines, provide faster access to new medicines that are safe and effective, and support the development of tools for more appropriate prescribing. To support these actions, Budget 2017 outlined an investment of $140.3 million over five years, starting in 2017–2018, and $18.2 million, for ongoing years. The proposed regulatory amendments contribute to this initiative with respect to the price of patented medicines.

*The Patented Medicine Prices Review Board ("PMPRB" or "the Board")*

The PMPRB was created in 1987 as the consumer protection "pillar" of a major set of reforms to the *Patent Act* ("Act"), which were designed to encourage greater investment in medicine R&D in Canada through stronger patent protection. The Act sets out the period of time that patentees of a medicine are provided the exclusive rights granted by a patent. It also establishes the PMPRB as a quasi-judicial body with a price regulatory mandate to ensure that patentees do not abuse their patent rights by charging consumers excessive prices during this statutory monopoly period.

The Act and the *Patented Medicines Regulations* ("Regulations") together form the patented medicines price regulatory framework of the PMPRB. Regulations with respect to patented medicine prices and information are made pursuant to the Minister's recommendation; however, the PMPRB carries out its regulatory mandate at arm's length from the Minister.

## *The* Patent Act *and* Patented Medicines Regulations

Although no definition of "excessive" is included in the regulatory framework, it does specify the factors and information that the Board must consider in determining whether a price is excessive. The current price regulatory factors as set out in section 85 of the Act are the following:

- The prices at which the same medicine has been sold in the relevant market;

- The prices at which other medicines in the same therapeutic class have been sold in the relevant market;
- The prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada; and
- Changes in the Consumer Price Index.

The Regulations specify the price information that patentees must report to the PMPRB to allow it to regulate prices and report on trends. They include requirements to report the identity and price information for patented medicines sold in Canada and their prices in seven foreign countries where they are also sold. Currently the seven countries set out in the schedule to the Regulations (the PMPRB7) are the United States, the United Kingdom, France, Germany, Switzerland, Italy and Sweden. Although section 85 of the Act allows for further price regulatory factors to be prescribed in the Regulations, none have been proposed for consideration until now.

## *The PMPRB's* Compendium of Policies, Guidelines and Procedures

Many of the core regulatory concepts in the Act and the Regulations have been further developed in, and are operationalized through, guidelines. The PMPRB is authorized to make non-binding guidelines under section 96 of the Act, subject to consultation with relevant stakeholders. The purpose of the guidelines is to establish, and ensure that patentees are generally aware of, the policies and procedures undertaken by the Board staff to identify the medicines that might be priced excessively.

#### *How the current regulatory framework works*

Under the PMPRB's current regulatory framework, as operationalized through the guidelines, new patented medicines are assessed for the degree of therapeutic benefit they provide relative to existing medicines on the market. Depending on the outcome of that process, the PMPRB determines a price ceiling for new patented medicines that is based either on the median price of that same medicine in the PMPRB7 countries, the highest-priced medicine in Canada in the same therapeutic class, or some combination of the two. Once a patentee sets a medicine's introductory price in relation to that ceiling and it enters the market, the PMPRB allows annual price increases in keeping with the Consumer Price Index (CPI), provided these increases do not make the Canadian price greater than the highest price of the same medicine among the PMPRB7 countries.

The PMPRB's current regulatory framework is operationalized by Board staff who investigate medicines that appear to be priced excessively. Board staff apply the tests and thresholds specified in the guidelines to each patented medicine sold in Canada, notify the patentee that they are under investigation if the prices fail those tests and thresholds, and try to negotiate a voluntary compliance undertaking (VCU) by the patentee based on the compliant price level as set out in the guidelines. A VCU is a written commitment by a patentee to comply with the PMPRB's guidelines, including adjusting the price of the patented medicine in question to a level that complies with the guidelines and offsetting any potential excess revenues that may have been received as the result of having sold the patented medicine at a non-guideline compliant price in Canada.

If an acceptable VCU is not concluded, the case proceeds to a public adversarial hearing in front of a panel composed of members of the Board. During a hearing, the Board panel acts as a neutral arbiter between the parties (Board staff and the patentee). The Board panel must consider every factor under subsection 85(1) in determining whether the price of a medicine sold in Canada is excessive. The Board panel is not

bound by the guidelines during a hearing, although the Board staff, when presenting evidence in front of the Board, often relies on tests and methods that appear in the guidelines as part of its case that the medicine has been sold at an excessive price. If the Board panel determines that the medicine was sold at an excessive price, it may issue an order to enforce a non-excessive price and order the patentee to repay any excess revenue that resulted from selling the drug at an excessive price. An order of the Board can be enforced in the same manner as an order of the Federal Court.

*Canada's changing market and rising medicine costs*

Since the establishment of the PMPRB three decades ago, the medicine market has changed significantly. Medicine development is increasingly focussed on higher-cost medicines, such as biologics, genetic therapies targeted to smaller patient populations and medicines for rare diseases. The risk of asserting market power through excessive pricing is often greater for these products since there are few, if any, substitutes, and the patentee is not subject to competition. This is especially true for medicines that are first of their kind, or for which alternatives are less effective or have less tolerable side effects.

The current market dynamic has contributed to a significant increase in the cost of medicine in Canada which, if left unaddressed, is expected to continue. Between 2005 and 2016, the number of medicines in Canada with annual per-patient treatment costs of at least $10,000 increased from 20 to 135. This represents between 30% and 40% of new patented medicines coming under the PMPRB's jurisdiction each year and is a dramatic increase in these types of medicines over a brief timeframe. In 2015, 20 medicines had annual per-patient treatment costs over $50,000. High-cost specialty medicines now account for nearly one quarter of public and private insurer costs, but less than 1% of their beneficiaries.

Canadian patented medicine prices are among the highest in the world. Of all 35 Organisation for Economic Co-operation and Development (OECD) member countries, only the United States and Mexico have higher patented medicine prices than Canada. In 2015, median OECD prices for patented medicines were on average 22% below those in Canada.

*Confidential price adjustments*

Medicine manufacturers increasingly negotiate price adjustments with insurers in exchange for having their products reimbursed through insurance plans. These price adjustments are typically negotiated in confidence, with the agreement that they not be disclosed publicly. This means that there is a growing discrepancy between public list prices and lower actual prices paid in the market due to the increased use of confidential price adjustments.

*Limitations of current price regulation*

For the past 20 years, many countries that set price limits on medicines have relied on international price comparison between countries. With the emergence of higher-cost medicines, coupled with confidential price adjustments, countries have had to modernize with new methods that, for those medicines, are more reliant on assessing the economic value of a new medicine to their respective health systems and less on comparing prices internationally. Between 2010 and 2012, 23 European countries began planning or executed significant reforms to their regulatory frameworks for patented medicine prices. While international price comparison is still widely used in international price regulation, it is increasingly used as an adjunct to other pricing factors.

*Price regulatory factors*

Section 85 of the Act sets out the price regulatory factors that the Board must consider in determining whether a medicine is being or has been sold at an excessive price in Canada. The current price regulatory factors direct the Board to consider the prices at which a medicine or other medicines in the same therapeutic class have been sold in other countries. The PMPRB relies upon public prices when making price comparisons internationally; however, these public prices do not reflect the confidential price adjustments negotiated with some insurers that have become systemic in Canada and around the world. In an era marked by high-cost specialty medicines, the level of confidential price adjustments negotiated can be substantial. This means that there is a growing discrepancy between public list prices and lower actual prices paid in the market and leaves the PMPRB to regulate on the basis of public prices that bear less and less resemblance to what insurers are actually paying in the market. The PMPRB needs other factors that it can use to assess whether a price is excessive.

*The schedule of comparator countries*

The schedule to the Regulations sets out the seven countries for which patentees are to submit price information. The PMPRB uses the prices of the same patented medicines in these countries, where available, to set price limits on medicine prices in Canada at introduction and in subsequent years. The schedule of countries to the Regulations has not been updated since the Regulations were first conceived 30 years ago. At that time, policy makers believed that patent protection and price were key drivers of medicine R&D investment. The choice was made to offer a comparable level of patent protection and pricing for medicines as existed in countries with a strong medicine industry presence, on the assumption that Canada would come to enjoy comparable levels of R&D. However, the percentage of R&D-to-sales by patentees in Canada has been falling since the late 1990s and is currently less than Canada obtained at the time of the 1987 *Patent Act* reforms. By comparison, and despite Canada having among the highest patented medicine prices, industry R&D investment relative to sales in the PMPRB7 countries is on average 22.8% versus 4.4% in Canada. As a result, there is no evidence of a determinant link between domestic prices and the location of industry R&D investment. Other factors, such as head office location, clinical trials infrastructure and scientific clusters, appear to be much more influential determinants of where medicine investment takes place in a global economy.

The policy intent of the original schedule selection has not materialized and is no longer considered to be the most appropriate basis for the composition of the countries listed in the schedule. The regulatory requirements for patentees to report on prices in the PMPRB7 keep Canadian prices for patented medicines among the highest in the world.

## Issues

The Board determines whether a price is excessive based on the price regulatory factors in the Act, and the patentee price information reporting requirements specified in the Regulations. The evolution in the global and Canadian medicine environment has made apparent two important limitations to the Board’s current regulatory framework: (1) the ineffectiveness of the current price regulatory factors to adequately inform the PMPRB’s assessment of excessiveness; and (2) the insufficiency of the patentee price information reporting requirements.

Under the current regulatory framework, excessiveness is assessed almost entirely on the basis of domestic and international public list prices. This is problematic with an influx in high-cost specialty medicines and list prices not reflective of what public and private insurers are actually paying. The main limitations of the current framework are that

- It does not provide additional price regulatory factors, beyond price comparisons and CPI, for the PMPRB to assess whether a price is excessive. It does not consider whether the price of a medicine reflects
- **The value of a medicine to a patient:** medicines that offer substantial clinical benefits to patients or are alone in their therapeutic class will be in greater demand than medicines that are only marginally better than the standard of care or are one among many in their class;
- **The number of patients that can benefit from a medicine:** the size of the market for a medicine can have an impact on its expected price and the ability to pay for the medicine in a given country; and
- **The wealth of a country:** countries with greater economic resources can afford more or higher-cost medicines than countries with fewer resources.
- The list of countries used for price comparisons (PMPRB7) is out of date. Canadian prices for new medicines are compared to those of countries with high medicine prices, rather than to those of countries with similar medicine markets, consumer protection and wealth. The selection of countries can have a significant impact on the price maximums for patented medicines in Canada. As the PMPRB relies on international price comparisons, the PMPRB7 set of comparator countries has the effect of allowing higher prices in Canada than would otherwise be the case if comparator countries were more reflective of the Canadian medicine market.

### Objectives

The proposed amendments to the *Patented Medicines Regulations* would ensure that the PMPRB is equipped with the price regulatory factors and patentee price information reporting requirements necessary to fulfill its mandate to protect Canadian consumers from excessive prices for patented medicines. It is anticipated that the implementation of these amendments by the PMPRB would lead to lower prices for patented medicines in Canada that are more closely aligned with their value to patients and the health care system, and Canadians' willingness and ability to pay.

### Description

There are five elements included in the proposed amendments.

## Price regulatory factors and updating the schedule of comparator countries

1. Introduce new, economics-based price regulatory factors that would enable the PMPRB to ensure non-excessive prices that reflect value and Canada's willingness and ability to pay for patented medicines.

2. Update the schedule of countries used by the PMPRB for international price comparisons to be better aligned with the consumer protection mandate of the PMPRB and median OECD prices.

## Reporting requirements

3. Reduce reporting obligations for patented veterinary, over-the-counter and "generic" medicines.

4. Set out the information reporting requirements to enable the PMPRB to operationalize the new price regulatory factors.

5. Require patentees to report price and revenue information that is net of all domestic price adjustments such as direct or indirect third party discounts or rebates and any free goods or services.

A more detailed description of each of the proposed amendments follows.

## 1. Introduce new, economics-based price regulatory factors that would ensure prices reflect value and Canada's willingness and ability to pay for patented medicines

This proposed amendment would introduce three additional price regulatory factors of pharmacoeconomic value, market size, and gross domestic product (GDP) and GDP per capita in Canada. These new price regulatory factors would enable the PMPRB to consider complementary and highly relevant aspects of price excessiveness related to the value of the health benefit produced by the medicine, and the willingness and ability of Canadian consumers to pay for it. These new factors will only apply to sales of patented medicines that occur after the coming into force of the proposed amendments.

*Pharmacoeconomic value of the medicine in Canada*

The price paid for a medicine should take into consideration the value it produces. At the same time, it must recognize the cost to supply the medicine if manufacturers of medicines are to continue to invest in the production of new medicines. A pharmacoeconomic evaluation identifies, measures, and compares the costs and benefits of a given medicine to patients and the health care system. The inclusion of this factor would require the Board to consider whether a medicine's price is commensurate with the benefits it provides to patients within the context of the Canadian health care system.

*Size of the market for the sale of the medicine in Canada and in countries other than Canada*

The addition of this factor in the Regulations could enable the PMPRB to develop market impact tests for medicines that are likely to pose affordability challenges for insurers due to the market size for the medicine. The impact of an excessive price is a function of both price and volume; the larger the size of the market for the medicine in Canada, the greater the impact of its price. Where public and private insurers are called on to cover the cost of a medicine for a significant number of patients, the high cost of a medicine could render the medicine unaffordable for all who need it. The Canadian price could be assessed against international prices and prevalence (number of people with the disease) levels in an effort to evaluate the price-volume relationship and establish a reasonable market impact test. Including the size of the market as a factor would also allow the PMPRB to reassess the prices of patented medicines over time. Once a medicine is on the market, the patentee may seek regulatory approval from Health Canada to use the medicine in the treatment of other conditions, or the medicine might also be prescribed by physicians off-label (i.e. prescribed for the treatment of conditions for which the medicine has not received regulatory approval). Since patented medicines are protected from new entrants, their prices can remain unaffected from subsequent fluctuations in the size of the market into which they may be sold. As patentees are assumed to set their introductory prices at a profitable level to recoup initial investment, a growth in the market size should align and correct prices downwards to a comparable level. Failure to do so could suggest that the original price, for an expanded market, is now excessive.

*GDP in Canada and GDP per capita in Canada*

The GDP is a measure of a country's economic output. GDP growth measures how much the inflation-adjusted market value of the goods and services produced by an economy is increasing over time. Per capita GDP measures how much a country is producing relative to its population. Growth in Canadian GDP can be taken as an indicator of the country's ability to pay year-over-year, whereas per capita GDP is a proxy for buying power at the level of the individual. The introduction of GDP in Canada and GDP per capita in Canada as a price regulatory factor would provide the PMPRB with measures of ability to pay for medicines at the national and individual level. The inclusion of this factor would allow the PMPRB to assess the impact of a medicine's price on the finances of consumers and insurers. It could also enable the PMPRB to develop market impact tests for medicines that are likely to pose affordability challenges for insurers due to the market size for the medicine.

## 2. Update the schedule of countries used by the PMPRB for international price comparisons to be better aligned with the PMPRB's consumer protection mandate and median OECD prices

The PMPRB uses the publicly available list prices of patented medicines sold in the PMPRB7 to set maximum prices for the same patented medicines in Canada at introduction and in subsequent years. Depending on their price levels, the selection of countries can have a significant impact on the maximum prices for patented medicines in Canada.

This proposed amendment would reconsider the PMPRB7 to update the list of countries set out in the schedule to be better aligned with the PMPRB's consumer protection mandate, and Canada's wealth and status as a major market for medicines. The scope of countries considered for the revised schedule was the 35 OECD countries, as they share the same economic and social policies as Canada. Requiring patentees to report on prices in all 35 member countries was deemed unnecessary because (1) this would present a significant reporting burden; (2) some OECD countries are better aligned with Canada's domestic policy priorities and economic standing; and (3) it may be difficult to obtain price and sales information from some countries. Three criteria were used to select a subset of OECD countries to form the revised schedule.

First, the countries must have medicine pricing policies that are well aligned with the consumer protection mandate of the PMPRB, such as a country having national pricing containment measures to protect consumers from high medicine prices. For example, the United States does not satisfy this criterion.

Second, countries must possess reasonably comparable economic wealth as Canada, such as a country having a similar economic standing to Canada, as measured by GDP per capita. This is to ensure that prices correspond to Canada's ability to pay for medicines. For example, Canada's GDP per capita ranks eleventh among OECD countries, but prices for patented medicines are the third highest. The proposed schedule includes countries that have reasonably higher, similar and lower GDP per capita as Canada.

Third, countries are required to have a similar medicine market size characteristics as Canada, such as population, consumption, revenues and market entry of new products. This is to ensure that the resulting similar-sized markets produce a price level that is commensurate with Canada's share of global medicine sales.

Using these criteria, the proposed schedule lists Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, South Korea, Spain, Sweden and the United Kingdom (PMPRB12). Including a larger number of countries in the schedule would make price tests less sensitive to the influence of countries with

prices that are high or low, and reduce the impact where price and sales information is delayed or not available. For example, with only seven reference countries, delayed or missing price information from just two of the reference countries could impact the sample median by as much as 10%. Increasing the schedule to 12 countries would reduce this impact to just 2%. This slightly larger list would provide the PMPRB with a more balanced perspective of prevailing market prices and greater stability of the sample median without imposing significantly greater reporting requirements on patentees or administrative burden on the PMPRB.

### 3. Reduce reporting obligations for patented veterinary, over-the-counter and "generic" medicines

The Regulations currently only require patented veterinary and over-the-counter medicines (that do not contain a controlled substance or are not a radiopharmaceutical or biologic as per the *Food and Drugs Act* and the *Food and Drug Regulations*) to report price and sales information to the PMPRB on a complaints basis. Proposed amendments would further reduce reporting obligations for these medicines so that price, sales, and identity information would only be required on request by the PMPRB for all patented veterinary and over-the-counter medicines, including those that may contain a controlled substance, or are a radiopharmaceutical and/or a biologic. Amendments would also extend the same reduced reporting obligations to patented generic medicines (i.e. medicines approved by means of an ANDS). Patentees of generic medicines typically face greater competition, and the risk of excessive pricing due to market power is generally not cause for concern. These proposed amendments are intended to spare patentees unnecessary reporting regulatory burden for medicines that pose a lower risk of excessive pricing. It would also allow the PMPRB to focus its resources on medicines that pose a more substantive risk of excessive pricing.

### 4. Set out the patentee pricing information reporting requirements to enable the PMPRB to operationalize the new pricing factors

The current Regulations specify what information patentees must provide to the PMPRB in support of the current price regulatory factors. This includes information about the prices of patented medicines sold in Canada and other countries, patentees' revenues and R&D expenditures. Patentees would be required to report new information to the PMPRB to support the new pharmacoeconomic value and market size factors. Patentees would not be required to report on information related to GDP and GDP per capita, as this information would be obtained from Statistics Canada.

Information regarding pharmacoeconomic value: patentees would be required to provide the PMPRB with all published cost-utility analyses that express the value in terms of the cost per quality-adjusted life year (QALY). Cost-utility analyses are viewed by experts as the "gold standard" approach to considering the economic value of new medicines. The cost per QALY quantifies benefit by measuring lengthened life and/or improved quality of life. It is the most established measure of pharmacoeconomic value, as it enables comparisons across different types of medicines by using a common unit of measurement. This information reporting requirement would enable the PMPRB to consider the introduction of the concept of a maximum cost per QALY threshold in Canada.

In recognition of the significant expertise that can be necessary to prepare and validate cost-utility analyses, reporting would be limited to those that have been prepared by a publicly funded Canadian organization, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or the Institut

national d'excellence en santé et services sociaux (INESSS). These organizations have dedicated expertise, and they generally conduct pharmacoeconomic analyses for medicines seeking to be reimbursed by public insurers. The PMPRB would consider these analyses in its evaluation of price excessiveness. It would not duplicate the work conducted by CADTH and INESSS as part of reimbursement processes.

Even though the new pharmacoeconomic value factor would only apply to sales of patented medicines made after the coming into force of the amended Regulations, the obligation to submit the most recently published cost-utility analysis would extend to all patented medicines, both those marketed as of the date of the amended Regulations coming into force and any new medicines offered for sale following the date of the coming into force. Cost-utility analyses are typically only prepared for a given medicine following certain trigger points in a medicine's life cycle (e.g. at time of initial market launch or following regulatory approval for use of the medicine in the treatment of a new condition). Although the most recent cost-utility analysis for an existing medicine could be several years old, it would still reflect the most recent and relevant information for the PMPRB to consider when applying the new factor of pharmacoeconomic value. Patentees would only be required to provide published analyses — there would be no obligation on the patentee to prepare a cost-utility analysis if one does not exist.

Information respecting market size: patentees would be required to provide the PMPRB with information on the estimated maximum use of the medicine in Canada, by quantity of the medicine sold in final dosage form, for each dosage form and strength that are expected to be sold. It is expected that patentees already construct this estimate as part of their development plans to introduce a new patented medicine to the Canadian market. Patentees compile this information in the development of business plans and for CADTH processes. Before going to market, patentees rely upon available statistics and information on the prevalence (number of people with a disease) in a given country and incidence (estimated number of new cases each year) to develop a sales forecast. They also take into account other factors such as competition to estimate the potential market share for their new medicine.

Patentees would also be required to provide the PMPRB with updated estimates that may occur, for example, when a medicine receives approval from Health Canada for use in the treatment of a new condition that expands the estimated market for the medicine. The new factor of market size would only apply to sales of patented medicines made after the coming into force of the amended Regulations. However, in view of the fact that it can take up to three years for the market for a new medicine to fully mature, patentees of medicines that are already on the market and were first offered for sale within three years prior to the amended Regulations coming into force or have received regulatory approval for use in the treatment of a new condition within this same three-year period would be required to provide information on the estimated maximum use of these medicines in Canada.

## 5. Require patentees to report price and revenues, net of all price adjustments

The Regulations currently require patentees to report information on price adjustments for the first point of sale only. Patentees are not required to report the significant price adjustments they may provide to third party insurers such as provincial insurers that provide reimbursement for the cost of a medicine sold to a patient. Provincial insurers are some of the biggest payers of patented medicines in Canada. Without this information, the PMPRB sets the non-excessive price maximum of a medicine on the basis of information that only includes some price adjustments. This amendment would require patentees to report price and revenue information that is net of any price or other adjustments, including discounts, rebates and free goods and services, to any party that pays for, or reimburses, the medicine. Although most adjustments are

likely to result in a price reduction, this amendment is intended to capture information on any adjustment including those resulting in a price increase. This information would be considered privileged as per section 87 of the *Patent Act* and would be considered by the Board when determining excessiveness.

With this information, the PMPRB would use the price that is net of any price adjustments to calculate the non-excessive price maximum. The PMPRB currently regulates the non-excessive price of a medicine based on the prices of other medicines in the same therapeutic class for sale in Canada. Since that price information does not include third-party price adjustments, the prices of comparator products that subsequently enter the market are often inflated (as the price ceilings for those medicines are determined in relation to an inflated list price of the existing medicine, rather than the actual price paid in Canada). As a result, the therapeutic class comparison tests yield price maximums that are higher than they would be if the actual price paid were available to the PMPRB. Compelling actual price information, inclusive of all price adjustments provided by the patentee, would allow the PMPRB to include rebates in the calculation of the average transaction price. It would also provide a mechanism for patentees to comply with the regime by calculating a true transaction price reflective of all rebates and discounts, direct and indirect.

## Regulatory and non-regulatory options considered

Status quo

The option of taking no action was considered and rejected on the grounds that the PMPRB's current regulatory framework lacks effective price regulatory factors and sufficient patentee price information reporting requirements. The current factors do not take into account all the aspects of excessiveness for new categories of medicines that have emerged since the creation of the PMPRB. The PMPRB's current patentee price information reporting requirements produce incomplete domestic pricing information and provide international price information from a number of countries with high patented medicine prices that are not equivalent to the Canadian market.

Non-regulatory modernization (updates to the PMPRB's *Compendium of Policies, Guidelines and Procedures*)

This option would be primarily limited to revised price tests that continue to rely completely on domestic and international price referencing methods. This option was fully explored, and included a stakeholder consultation by the PMPRB in 2016, but was rejected on the grounds that simply updating the guidelines does not address the underlying inadequacies of the existing Regulations. Regulatory reform is needed to obtain all price adjustment information and lessen the current dependence on international price testing through the addition of new factors. Under a modernized regulatory framework, the PMPRB would have a stronger basis from which to modernize its guidelines.

## Benefits and costs

The quantitative benefits from the cost-benefit statement relate to lower overall spending on patented medicines in Canada that is anticipated to result from lower prices. The quantified costs relate to (1) reduced industry revenues due to lower prices for patented medicines; (2) the net impact of new and reduced administrative industry reporting requirements; and (3) the costs to the Canadian government to ensure compliance with the proposed amendments.

The total quantified benefit of lower patented medicine prices is estimated at $21.3 billion (PV) over 10 years. The total quantified cost of this proposal, including all of the industry's lost revenues, is estimated at $8.6 billion (PV) over 10 years. Administrative costs to industry and the Government of Canada are anticipated to be approximately $62 million (PV) over 10 years. The total net benefits of the proposed amendments are estimated to be $12.7 billion (NPV) over 10 years, from 2019 to 2028. A discount rate of 7% was used in all PV calculations. The complete cost-benefit analysis is available upon request.

*Cost-benefit statement*

| **Quantified impacts** (*CAN$, 2017 price level/constant dollars*) | | | | |
|---|---|---|---|---|
| | **Base Year (Year 1)** | **Final Year (Year 10)** | **Total (PV)** | **Annualized Average** |
| **Benefits** | | | | |
| Lower drug expenditure | $219,993,857 | $2,782,694,694 | $8,567,004,599 | $1,219,745,515 |
| • New factors | $33,443,984 | $1,399,184,431 | $3,763,190,611 | $535,792,273 |
| • Updated schedule | $138,187,981 | $770,272,294 | $2,788,004,256 | $396,948,040 |
| • Third-party price adjustments | $48,361,892 | $613,237,969 | $2,015,809,732 | $287,005,201 |
| Health care system | $425,688,113 | $5,384,514,233 | $12,722,001,829 | $1,811,322,089 |
| **Total benefits** | $645,681,970 | $8,167,208,927 | $21,289,006,428 | $3,031,067,604 |
| **Costs** | | | | |
| Industry | | | $8,567,068,356 | $1,219,754,583 |
| • Loss revenues | $219,993,857 | $2,782,694,694 | $8,567,004,599 | $1,219,745,515 |
| • Administrative cost (includes regulatory burden reduction) | | | $34,717 | $4,924 |
| • Compliance cost | | | $29,106 | $4,144 |
| Government | $4,981,481 | $8,025,361 | $61,716,822 | $8,787,064 |
| • PMPRB program expenditure | $3,849,215 | $5,680,633 | $43,361,629 | $6,173,704 |
| • Special purpose allotment | $981,481 | $2,025,361 | $16,119,394 | $2,295,033 |
| • Accommodation requirements | $143,085 | $304,667 | $2,131,142 | $303,425 |
| • IT services | $7,700 | $14,700 | $104,657 | $14,900 |
| **Total costs (PV)** | | | $8,628,785,178 | $1,228,541,647 |

| | | |
|---|---|---|
| **Net benefits (NPV)** | $12,660,221,250 | $1,802,525,957 |
| Qualitative impacts | | |
| • Greater population health and increased savings to the health care system due to fewer acute care incidents. Lower prices could result in lower patient cost-related non-adherence to needed medicines (for example not filling prescriptions or skipping doses).<br>• Providing the opportunity to improve access to drugs and reallocate resources to other important areas of the health care system.<br>• Reduction in the burden placed on price negotiating bodies (e.g. the pan-Canadian Pharmaceutical Alliance) to ensure system affordability.<br>• Potential impact on wholesalers, distributors, pharmacies, and generic medicine manufacturers whose markups and prices are often expressed as a percentage of patented medicines prices. | | |

Costs

Patentee price information reporting requirements already exist under the current regulatory framework. For the most part, the types of information to be reported and the reporting frequency would remain unchanged. The increased administrative burden on the industry would be to report in relation to the new price regulatory factors. The proposal also includes the benefit of reduced administrative burden for certain types of medicines (patented over-the-counter, veterinary, and ANDS-approved medicines), but this reduction would not be sufficient to fully offset the new reporting requirements.

*Industry*

Industry costs would include the

- Reporting requirements on the new price regulatory factors. Patentees would ensure that the information be updated as new analyses are undertaken. Total administrative costs to report in relation to the new price regulatory factors are estimated to be $6,175 annually or $43,373 in PV over 10 years.
- Compliance cost to update reporting systems to include the proposed schedule of countries on which patentees must report pricing information every six months, and updating their domestic prices and net revenues to include all price adjustments. Patentees already have reporting systems in place for domestic and international prices — the proposal only modifies the type of information to be reported. Total compliance costs are estimated to be $4,144 annually or $29,106 in PV over 10 years.

*Administrative burden reduction*

The proposal removes the need for patented veterinary, over-the-counter, and generic drugs to file identity and price information with the PMPRB, unless that information is requested by the PMPRB. There are 96 medicine products (out of PMPRB's 1 359) that fall into these categories and are currently required to file information with the PMPRB. Given that the Federal Court of Appeal only recently clarified and upheld the PMPRB's jurisdiction over these medicines, the compliance for reporting of these medicines has not historically been considered by the PMPRB. Assuming full compliance, the administrative burden reduction is expected to be $8,656 (PV) over 10 years.

*Lost revenues to the medicine industry*

The PMPRB only regulates excessive patented medicine prices in Canada. Any price reduction and repayment of excess revenues that would occur as a result of this proposal would be pursuant to a voluntary compliance undertaking (VCU) by the patentee to comply with the new maximum compliant price levels, or pursuant to a Board Order made following a public hearing before the Board where a Board Panel determines that the medicine has been sold at an excessive price. It is estimated that this proposal will result in reduced industry revenues of approximately $8.6 billion (PV) over 10 years, due to reduced thresholds for maximum non-excessive prices in Canada. For the purpose of this cost-benefit analysis (CBA), national treatment of revenue was given to all patented medicine manufacturers in Canada, despite the fact that 90% of the companies that report to the PMPRB are multinational enterprises (MNEs).

*Government of Canada*

*Increasing the PMPRB's capacity*

Costs to Government would include funds for the PMPRB to hire additional staff to support the expected increase in enforcement-related activities, and to administer the new price regulatory factors. The base (2018–19), second (2019–20), third (2020–21), and fourth years (2021–22) would be anticipated to cost $3.8 million, $5.7 million, $6.7 million, and $7.7 million, respectively. From the fifth year onwards, it is anticipated that costs to Government would be $5.7 million/year to maintain the PMPRB's increased capacity.

*Increasing special purpose allotment funding*

With the proposed new Regulations in place, patentees might be less willing to offer voluntary compliance undertakings and instead press for formal and potentially prolonged hearings. The PMPRB would require additional funding for its special purpose allotment (SPA) to cover the costs of outside legal counsel and expert witnesses. Patentees might also more frequently challenge decisions made under the new regime in the Federal Court. The base (2018–19), second (2019–20), third (2020–21), and fourth years (2021–22) would be anticipated to cost $1.0 million, $1.8 million, $2.8 million, and $3.8 million, respectively. From the fifth year onwards, it is anticipated that costs to Government would be $2.0 million/year to maintain the PMPRB's increased SPA funding.

*Offsetting costs to Public Service and Procurement Canada and Shared Services Canada*

Increasing the PMPRB's staffing levels would also increase accommodation and information technology (IT) costs. Combined, the base (2018–19), second (2019–20), third (2020–21), and fourth years (2021–22) would be anticipated to cost $151,000, $305,000, $328,000, and $331,000, respectively. From the fifth year onwards, it would be anticipated that costs to Government would be $319,000/year to offset Public Service and Procurement Canada's accommodation costs and Shared Services Canada's IT services costs.

The total cost to the Government of Canada would be anticipated at $61.7 million in net present value over 10 years.

Benefits

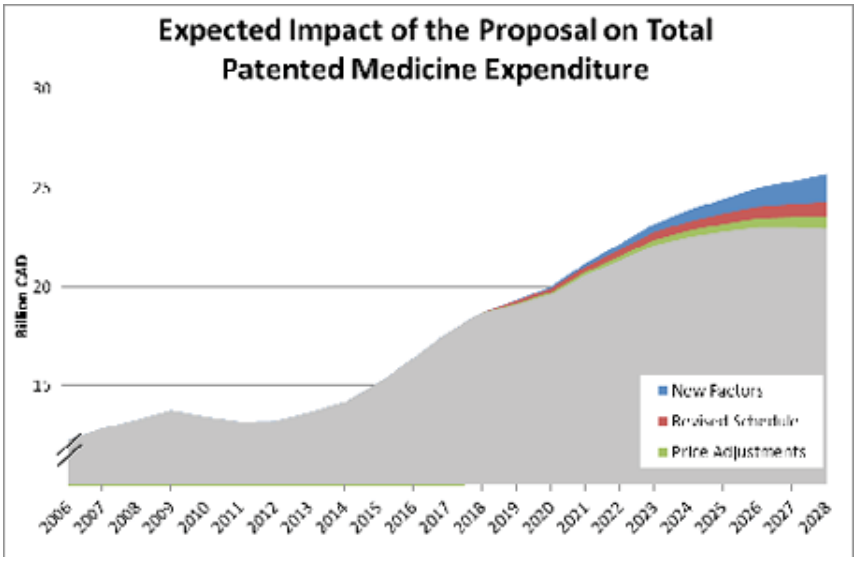
Benefits were calculated based on the expected reduction in the level of public risk of excessively priced patented medicines in Canada.

Anticipated quantitative benefits were calculated on the basis of reduced overall spending on patented medicines. The projected baseline of future spending (2017–2028) was calculated using current growth trends and anticipated launches from the current medicine pipeline. It also includes the expected loss of patent protection of medicines that are currently under the PMPRB's jurisdiction. The total net benefits arising from the proposed amendments are estimated to be $25.1 billion dollars (NPV) over 10 years.

## Lower patented medicine expenditure

The proposed amendments are expected to lower patented medicine expenditure by an estimated $8.6 billion (PV) over 10 years.

The introduction of the new price regulatory factors would be expected to have the biggest impact on patented medicine expenditure ($3.8 billion), followed by the revised schedule ($2.8 billion) and the reporting of price and sales adjustment with third parties ($2.0 billion).




*Healthcare system benefits*

Without the proposed amendments, it is estimated that public health care systems from across Canada will spend an additional $3.9 billion (PV) for the same quantity of patented medicine. This represents a significant opportunity cost for the Canadian public health care system, as these funds could have been used in other areas of the health care system to better the health of Canadians. Given the large ripple effects on health and the economy for every dollar spent in public health, (see footnote 1) the size of this opportunity cost in Canada is quite substantial. The total opportunity cost to the health care system of paying for excessively priced medicines was estimated to be $12.7 billion dollars (PV) over 10 years.

*Sensitivity analysis summary*

A sensitivity analysis was performed in relation to two variables that could greatly affect the estimated impact of the proposal. The first variable relates to the PMPRB implementation of the proposal and the other to the projected growth rate in patented medicine expenditure. The baseline analysis was conducted on an assumption that the PMPRB continues to apply price test methods that are similar to those currently in place. This assumption is necessary since any changes to the guidelines are fully within the control of the PMPRB. For example, the PMPRB currently uses the median PMPRB7 price to test new medicines against prices in other countries. The baseline assumes that the median price test would also be applied to the new

PMPRB12. The sensitivity analysis of this variable examined possible alternate approaches to the existing price regulatory factors as well as possible approaches to implementation of the proposed new factors in the guidelines.

The second variable relates to the growth of expenditures in patented medicines. If growth in patented medicine expenditure is higher than anticipated, the benefit measured in dollars, calculated from a percent reduction due to lower patented medicine prices, will be higher than anticipated. Likewise, if growth in expenditure is lower than anticipated, then the overall benefit will also be lower. Growth in the patented medicine industry is difficult to predict, and the emergence of new types of patented medicines, such as biologics, introduces new uncertainties into modelling efforts.

The sensitivity analysis demonstrates that total patented medicine expenditure could be lowered from a minimum of $6.4 billion dollars (PV) after 10 years to a maximum of $24.9 billion dollars (PV) after 10 years. The minimum sensitivity analysis impact represents the lowest projected patented medicine sales growth coupled with the least aggressive reforms to the PMPRB guidelines. The maximum sensitivity analysis impact represents the highest projected patented medicine sales coupled with the most aggressive reforms to the PMPRB guidelines. The current CBA estimates the baseline cumulative expenditure after 10 years to be $8.6 billion dollars (PV). (see footnote 2)

*Distributional analysis summary*

The vast majority of patented medicine manufacturers are located in Ontario, Quebec, British Columbia, and Alberta. These four provinces constitute 98% of all companies that would be affected by the proposed amendments.

All — public, private, and out-of-pocket — payers of patented medicines from across the country will benefit from lower prices.

Usage by age and gender: According to Statistics Canada's report "Prescription medication use by Canadians aged 6 to 79," prescription medicine use rose with age from 12% among 6- to 14-year-olds to 83% among 65- to 79-year-olds. Prescription medicine use was also associated with the presence of physical and mental health conditions. The percentage of Canadians taking prescription medicines did not differ by household income. Females were generally more likely than males to report taking prescription medications (47% versus 34%). However, at ages 6 to 14, a higher percentage of boys, rather than girls, used prescription medications, and at ages 65 to 79, the prevalence of prescription drug use was similar for men and women. Prescription drug use intensity — the number of different medications taken — was strongly associated with age. The percentage taking more than one medication rose from 3% at ages 6 to 14 to 70% at ages 65 to 79.

## "One-for-One" Rule

The estimated added regulatory burden to patentees was calculated to be approximately $43,373, with an estimated reduction in regulatory burden of $8,656, for a total of $34,717 (PV over 10 years). This calculation includes the upfront cost of providing the PMPRB with cost-utility and market size analyses for medicines currently under the jurisdiction of the PMPRB, the ongoing costs of updating these analyses and providing the PMPRB cost-utility analyses and market size estimates for all new patented medicines that enter the market, as well as further reducing the current reporting requirements for patented veterinary, over-the-counter medicines, and adding generic medicines to those same reduced reporting obligations. The proposal is considered an "IN" under the "One-for-One" Rule and has an estimated impact of $3,062.

| *Current initiative is an:* | *"IN" ("One-for-One" Rule)* | | |
|---|---|---|---|
| | **Values to Report in Regulatory Impact Analysis Statement** | **Rounding** | **Unit of Measure** |
| Annualized administrative costs (constant $2012) | $3,062 | 0 digits | Constant 2012 dollars, present value base year: 2012 |
| Annualized administrative costs per business ($2012) | $40 | 0 digits | Constant 2012 dollars, present value base year: 2012 |

## Small business lens

The small business lens does not apply to the proposed amendments, as only medicine manufacturers that have a patented medicine for sale in Canada would be affected by the proposed amendments. Among the 77 companies reporting to the PMPRB, none were identified as satisfying the small business definition. In general, patented medicines are sold by multinational enterprises or their subsidiaries.

## Consultation

The consultation period for prepublication in the *Canada Gazette*, Part I, of the regulatory proposal will be 75 days.

This consultation builds on an initial consultation on the regulatory proposal. On May 16, 2017, the Honourable Jane Philpott, former federal Minister of Health, announced the launch of the consultation on the proposed amendments to the *Patented Medicines Regulations.* A consultation document entitled "Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations" was posted on Health Canada's website as well as the Government of Canada's Consulting with Canadians website. The consultation was promoted through a news release and an email notification that was distributed widely to stakeholders. In addition, to comply with subsection 101(2) of the *Patent Act*, Minister Philpott wrote each of her counterparts in the provinces and territories, inviting comments on the proposed regulatory amendments. Written submissions from all stakeholders and interested parties were accepted until June 28, 2017. During the consultation period, Health Canada hosted nine engagement sessions with external stakeholders, including representatives from public and private insurers, patient organizations, the medicine industry, the health professions and academia.

Insurers (public and private) were supportive overall, noting that pharmacoeconomic value and market size are very relevant to the determination of price excessiveness. There was no consensus around GDP as a factor. Private insurers suggested that the factors account for considerations relevant to employers, such as the impact of the medicine on productivity, absenteeism, and disability claims. Insurers supported the revised schedule of countries. While in favour of reducing regulatory burden for patented generic medicines, insurers suggested that the PMPRB still request price and sales information for patented generics at risk of higher prices. Finally, insurers were supportive of the amendment to provide the PMPRB with price adjustment information, on the condition that this information remain confidential to the PMPRB.

Patient organizations noted that the high prices of new patented medicines pose a financial barrier to access for Canadians and asked that the Regulations ensure that patient access to medicines is a primary concern. Patient organizations suggested that there be enough flexibility in the Regulations to allow the PMPRB to go beyond the cost per QALY to take patient preferences into account and to consider special circumstances such as medicines for rare diseases. In addition, organizations asked that the use of price adjustment information in regulating prices not compromise the bargaining position of insurers.

Representatives of the brand name medicine industry suggested that proposed amendments would add significant complexity and uncertainty for patented medicines to reach the market in Canada. A number of representatives suggested that the proposed economic-based factors go beyond the mandate of the PMPRB and are potentially duplicative of CADTH's assessment. They expressed concern around the additional regulatory burden of providing international pharmacoeconomic and pricing information. A common suggestion was that the United States should remain in the schedule of countries. It was recommended that the Regulations allow for a risk-based approach and that regular reporting requirements should be removed for lower-risk products. It was not clear to the industry how the PMPRB plans to use and protect confidential price adjustment information; however, it was suggested that providing this information to the PMPRB would risk lower price adjustments for insurers in Canada.

Generic medicine industry representatives supported the proposal to remove the requirement for patented generic manufacturers to regularly report information about the identity and price of these medicines, as they pose a low risk of abusing market power and are subject to price regulation by the provinces and territories. They recommended this amendment be extended to include other complex forms of generics that do not receive a Declaration of Equivalence from Health Canada, such as biosimilars and generics with complex ingredients and formulations.

The consumer health products industry acknowledged that the over-the-counter products (OTCs) it produces are already exempt from reporting regularly. Representatives recommended that all self-care products be exempt entirely from the patented medicine framework; however, it is beyond the scope of the Regulations to change the PMPRB's jurisdiction over patented medicines.

Representatives from physicians' and nurses' associations supported economics-based factors to assess the value of a medicine, the revised schedule and requiring information on confidential rebates in Canada. Nurses' associations were not supportive of exempting patented generics from systematic reporting requirements. Pharmacists supported assessing a medicine based on its value, but noted that pharmacoeconomic value should consider benefits and costs beyond a QALY. They noted that the schedule of comparator countries should be revised based on the availability of products in each country and asked that the amendment pertaining to confidential price adjustments not compromise the price adjustments negotiated by public insurers.

Academics supported the proposed pharmacoeconomic value factor and cost per QALY information requirement. Some academics supported using GDP to set an upper bound on prices and suggested the use of per capita GDP. Academics were less convinced that market size information would be useful without more information on the R&D costs of a medicine. Most agreed with revising the schedule and removing countries that do not have consumer protections in place for excessive prices. Academics were generally in favour of allowing the PMPRB to collect information on adjustments in price, but they suggested it be broadened to include all types of transfers from patentees that impact prices, including pay-for-performance agreements, and cautioned against using rebate information when making international comparisons.

The responses related to the Regulations have been taken into consideration in the development of this proposal for prepublication in the *Canada Gazette*, Part I, and the Regulatory Impact Analysis Statement. In particular,

- The economics-based price regulatory factors in the proposed amendments have remained broad in order to provide the PMPRB with the flexibility to consider other measures beyond the cost per QALY where relevant, and to enable the PMPRB to develop appropriate measures using market size and GDP. Based on feedback received, GDP per capita has been added to the GDP factor.
- The information reporting requirements for patentees have been revised to minimize the regulatory burden while providing the PMPRB with sufficient information to protect Canadians from excessive prices. The proposed amendments do not require cost-utility analyses (CUAs) from countries other than Canada to be reported.
- Further analysis has been provided on the proposed schedule; an estimate of the impacts on patented medicine expenditures is provided in the cost-benefit analysis.
- Consideration was given to the removal of systematic information reporting requirements for patentees for other low-risk products beyond patented generic medicines. It is proposed that regular reporting requirements be removed for all patented over-the-counter medicines, including radiopharmaceuticals and biologics authorized for sale under the *Food and Drug Regulations* as well as those containing controlled substances. While other products such as biosimilars and other patented generic medicines that are not authorized for sale by way of an ANDS were considered, these products and their risk of excessive pricing could not be adequately defined.
- It is proposed that the new information reporting requirements in the Regulations capture all price adjustments that would serve to lower (e.g. discounts, rebates, free goods, free services) or raise (e.g. payment for performance) the price of a medicine.

### Regulatory cooperation

This proposal would update the schedule of countries used by the PMPRB for international price comparisons to be better aligned with the PMPRB's consumer protection mandate and median OECD prices. This international alignment would contribute to lowering medicine prices for Canadians.

### Rationale

Unlike most international health systems, Canada's health system does not have a single payer for medicines. Canadian expenditure on prescription medicines is split between public insurers (43%), private insurers (35%) and Canadians paying out-of-pocket (22%).

Modernization of the PMPRB's regulatory framework would benefit all those who pay for medicines in Canada through a higher standard of consumer protection. Canada's public and private insurers would benefit from lower maximum prices so their price negotiations achieve more than simply prices that match those in other countries. The amendments would help the PMPRB to achieve Canadian maximum prices closer to international norms. This would allow public and private insurers to negotiate with sellers on a more equal footing with health authorities in other countries. Employer-sponsored health insurance plans are anticipated to benefit from lower premiums and reduced risk of becoming untenable due to high-cost medicines. Uninsured Canadians who pay out-of-pocket for their medicines rely most heavily on the consumer protection mandate of the PMPRB, and they would benefit from lower prices for their patented medicines.

This proposal is anticipated to result in an estimated total benefit to Canadians of $8.6 billion in net present value (NPV) over 10 years following implementation.

### Implementation, enforcement and service standards

The proposed Regulations would come into force on January 1, 2019. This would allow patentees time to prepare for implementation of the new price regulatory factors and information reporting requirements on prices. January 1, 2019, was the date chosen to align the implementation with the PMPRB's reporting periods of January 1 and July 1. Once the amended Regulations are published in the *Canada Gazette*, Part II, responsibility for implementation, enforcement and service standards would be passed to the PMPRB. This is anticipated to include the finalization of a PMPRB-led stakeholder consultation on a revised *Compendium of Policies, Guidelines and Procedures* that will be used to reach an understanding of how the revised framework would be embodied in the form of specific price tests and qualifying information to be reported by patentees.

The new factors may only be considered in relation to sales that occur after the coming into force of the proposed amendments. However, the reporting requirements in the amended Regulations would be applied to new and existing patented medicines alike. Patentees of existing medicines would have 30 days after the coming into force to provide the cost-utility analysis (if available) and estimated market use information (if applicable). Price information for the countries in the revised schedule and domestic price and revenue information that takes into account price adjustments would first be required to be reported within 30 days after the end of the reporting period in which the proposed amendments came into force (i.e. within 30 days after June 30, 2019).

### Contact

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## PROPOSED REGULATORY TEXT

Notice is given that the Governor in Council, pursuant to subsection 101(1) (see footnote a) of the *Patent Act* (see footnote b), proposes to make the annexed *Regulations Amending the Patented Medicines Regulations*.

Interested persons may make representations concerning the proposed Regulations within 75 days after the date of publication of this notice. All such representations must cite the *Canada Gazette*, Part I, and the date of publication of this notice, and be addressed to Karen Reynolds, Executive Director, Office of

Pharmaceuticals Management Strategies, Strategic Policy Branch, Health Canada, 10th Floor, Brooke Claxton Building, 70 Colombine Driveway, Tunney's Pasture, Ottawa, Ontario K1A 0K9 (tel.: 613-957-1692; email: PMR-Consultations-RMB@hc-sc.gc.ca (mailto:PMR-Consultations-RMB%40hc-sc.gc.ca)).

Ottawa, November 23, 2017

Jurica Čapkun
Assistant Clerk of the Privy Council

# Regulations Amending the Patented Medicines Regulations

## Amendments

**1 Section 3 of the *Patented Medicines Regulations*** (see footnote 3) **is amended by adding the following after subsection (3):**

**(3.1)** Despite subsection (3), in each of the following cases, the information referred to in subsection (1) must be provided to the Board within 30 days after the day on which the Board sends a request for the patentee to provide that information:

**(a)** the medicine is not a *prescription drug* as defined in section A.01.010 of the *Food and Drug Regulations*;

**(b)** the medicine contains a *controlled substance* as defined in subsection 2(1) of the *Controlled Drugs and Substances Act*, the sale or provision of which does not require a prescription under that Act;

**(c)** a notice of compliance has been issued in respect of the medicine on the basis of information and material contained in a submission filed under section C.08.002.1 of the *Food and Drug Regulations*; or

**(d)** the medicine is for veterinary use.

**2 (1) The portion of subsection 4(2) of the Regulations before paragraph (a) is replaced by the following:**

**(2)** The information referred to in subsection (1) must be provided

**(2) Subsection 4(3) of the Regulations is replaced by the following:**

**(3)** Despite subsection (2), in each of the following cases, the information referred to in subsection (1), for each six-month period beginning on January 1 and July 1 of each year, must be provided to the Board within 30 days after the day on which the Board sends a request for the patentee to provide that information and, during the two years following the request, within 30 days after the end of each six-month period:

**(a)** the medicine is not a *prescription drug* as defined in section A.01.010 of the *Food and Drug Regulations*;

**(b)** the medicine contains a *controlled substance* as defined in subsection 2(1) of the *Controlled Drugs and Substances Act*, the sale or provision of which does not require a prescription under that Act;

**(c)** a notice of compliance has been issued in respect of the medicine on the basis of information and material contained in a submission filed under section C.08.002.1 of the *Food and Drug*

*Regulations*; or

**(d)** the medicine is for veterinary use.

**(3) Paragraphs 4(4)(a) and (b) of the Regulations are replaced by the following:**

**(a)** in calculating the average price per package of a medicine, the actual price obtained by the patentee must be used, taking into account any adjustments that are made by the patentee or any party that directly or indirectly purchases or reimburses for the purchase of the medicine and any reduction given to any party in the form of free goods, free services, gifts or any other benefit of a like nature; and

**(b)** in calculating the net revenue from sales of each dosage form, strength and package size in which the medicine was sold in final dosage form, the actual revenue obtained by the patentee must be used, taking into account any adjustments that are made by the patentee or any party that directly or indirectly purchases or reimburses for the purchase of the medicine and any reduction given to any party in the form of free goods, free services, gifts or any other benefit of a like nature.

**3 The Regulations are amended by adding the following after section 4:**

**4.1 (1)** For the purposes of paragraphs 80(1)(d) and (2)(d) of the Act, the information to be provided respecting the factor referred to in paragraph 4.4(a) is every cost-utility analysis prepared by a publicly funded Canadian organization, if published, for which the outcomes are expressed as the cost per quality-adjusted life year for each indication that is the subject of the analysis.

**(2)** The information referred to in subsection (1) must be provided

**(a)** if the information is published when the medicine is first offered for sale in Canada, within 30 days after the day on which the medicine is first offered for sale in Canada; and

**(b)** if the information is not published when the medicine is first offered for sale in Canada, within 30 days after the day on which it is published.

**(3)** Despite subsection (2), in the case of a medicine that is offered for sale in Canada before January 1, 2019, the information referred to in subsection (1) must be provided

**(a)** if the information is published before January 1, 2019, by January 30, 2019; and

**(b)** if the information is not published before January 1, 2019, within 30 days after the day on which it is published.

**(4)** If any other analysis as described in subsection (1) is published after those referred to in subsection (1) were provided, it must be provided within 30 days after the day on which it is published.

**4.2 (1)** For the purposes of paragraphs 80(1)(d) and (2)(d) of the Act, the information to be provided respecting the factor referred to in paragraph 4.4(b) is the estimated maximum use of the medicine in Canada, by quantity of the medicine in final dosage form, for each dosage form and strength that are expected to be sold.

**(2)** The information referred to in subsection (1) must be provided within 30 days after the day on which the medicine is first offered for sale in Canada.

**(3)** Despite subsection (2), in the case of a medicine that is offered for sale in Canada before January 1, 2019, the most recent version of the information referred to in subsection (1) must be provided

**(a)** if the medicine is first offered for sale in Canada during the period beginning on January 1, 2016 and ending on December 31, 2018, by January 30, 2019; and

**(b)** if the information referred to in subsection (1) in respect of the medicine is not required to be provided under paragraph (a), but the information is updated

**(i)** during the period beginning on January 1, 2016 and ending on December 31, 2018, by January 30, 2019; or

**(ii)** after December 31, 2018, within 30 days after the day on which it is updated.

**(4)** The information provided under this section must be up to date and any modification of that information must be provided within 30 days after the day on which the modification is made.

**4.3 (1)** Despite subsections 4.1(2) and (3) and 4.2(2) and (3), in each of the following cases, the information referred to in subsections 4.1(1) and 4.2(1) must be provided to the Board within 30 days after the day on which the Board sends a request for the patentee to provide that information:

**(a)** the medicine is not a ***prescription drug*** as defined in section A.01.010 of the *Food and Drug Regulations*;

**(b)** the medicine contains a ***controlled substance*** as defined in subsection 2(1) of the *Controlled Drugs and Substances Act*, the sale or provision of which does not require a prescription under that Act;

**(c)** a notice of compliance has been issued in respect of the medicine on the basis of information and material contained in a submission filed under section C.08.002.1 of the *Food and Drug Regulations*; or

**(d)** the medicine is for veterinary use.

**(2)** The requirements of subsections 4.1(4) and 4.2(4) apply in respect of the information provided under subsection (1).

### Other Factors to be Considered — Excessive Prices

**4.4** For the purposes of paragraph 85(1)(e) of the Act, the other factors that the Board must take into consideration to determine whether a medicine that is sold in any market in Canada after December 31, 2018 is being or has been sold at an excessive price are the following:

**(a)** the pharmacoeconomic value in Canada of the medicine and that of other medicines in the same therapeutic class;

**(b)** the size of the market for the medicine in Canada and in countries other than Canada; and

**(c)** the gross domestic product in Canada and the gross domestic product per capita in Canada.

4 **The schedule to the Regulations is replaced by the schedule set out in the schedule to these Regulations.**

### Coming into Force

**5 These Regulations come into force on January 1, 2019.**

## SCHEDULE

(Section 4)

## SCHEDULE

(Subparagraph 4(1)(f)(iii))

Australia
*Australie*

Belgium
*Belgique*

France
*France*

Germany
*Allemagne*

Italy
*Italie*

Japan
*Japon*

Netherlands
*Pays-Bas*

Norway
*Norvège*

Republic of Korea
*République de Corée*

Spain
*Espagne*

Sweden
*Suède*

United Kingdom
*Royaume-Uni*

[48-1-o]

Footnote 1

Reeves et al. “Does investment in the health sector promote or inhibit economic growth?” *Globalization and Health* (2013) 9:43.

Footnote 2
As per TBS guidelines, the discount rate used to calculate the net present value was 7%.

Footnote 3
SOR/94-688; SOR/2008-70, s.1

Footnote a
S.C. 2017, c. 6, s. 57

Footnote b
R.S., c. P-4

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# Government of Canada activities and initiatives

**#YourBudget2018 – Advancement**

(https://www.budget.gc.ca/2018/docs/themes/advancement-advancement-en.html?utm_source=CanCa&utm_medium=Activities_e&utm_content=Advancement&utm_campaign=CAbdgt18)
Advancing our shared values

**#YourBudget2018 – Reconciliation**

(https://www.budget.gc.ca/2018/docs/themes/reconciliation-reconciliation-en.html?utm_source=CanCa&utm_medium=%20Activities_e&utm_content=Reconciliation&utm_campaign=CAbdgt18)
Advancing reconciliation with Indigenous Peoples

**#YourBudget2018 – Progress**

(https://www.budget.gc.ca/2018/docs/themes/progress-progres-en.html?utm_source=CanCa&utm_medium=Activities_e&utm_content=Progress&utm_campaign=CAbdgt18)
Supporting Canada's researchers to build a more innovative economy

# Theoretical models of the cost-effectiveness threshold, value assessment, and health care system sustainability

March 2018

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**IHE White Paper**

# Theoretical models of the cost-effectiveness threshold, value assessment, and health care system sustainability

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## Acknowledgements

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## Corresponding Author

Please direct any inquiries about this report to Christopher McCabe, cmccabe@ihe.ca.

## Funding

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## Declared Competing Interest of Authors

Competing interest is considered to be financial interest or non-financial interest, either direct or indirect, that would affect the research contained in this report or create a situation in which a person's judgement could be unduly influenced by a secondary interest, such as personal advancement.

The authors of this publication claim no competing interest.

## Suggested Citation

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# Abbreviations

All abbreviations that have been used in this report are listed here unless the abbreviation is well known, has been used only once, or has been used only in tables or appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

| | |
|---|---|
| **CEA** | cost-effectiveness analysis |
| **DALY** | disability-adjusted life year |
| **GDP** | gross domestic product |
| **ICER** | incremental cost-effectiveness ratio |
| ***k*** | supply-side threshold |
| **λ** | threshold |
| **PCT** | primary care trust |
| **PMPRB** | Patented Medicine Price Review Board |
| **QALY** | quality-adjusted life year |
| **R&D** | research and development |
| ***v*** | demand-side threshold |
| **VSL** | value of a statistical life |
| **WTP** | willingness-to-pay |

# Table of Contents

# SECTION 1: Supply and demand-side models of the cost-effectiveness threshold, budget impact, and financial sustainability

Cost-effectiveness analysis (CEA) aims to assess the value of health gain attributable to a technology in order to assist the decision-makers in allocating scarce resources efficiently.[1] These analyses express costs in monetary units (such as dollars) and health gains in units of health such as quality-adjusted life years (QALYs) gained or disability-adjusted life years (DALYs) averted. Incremental cost-effectiveness ratios (ICERs) are calculated, which reflect the health gains compared to the costs incurred in providing the healthcare intervention. However, ICERs alone are not sufficient to inform policy decisions. A reference value is required to establish whether the ICER for a specific technology represents good or poor value;[2] this value is often referred to as the *cost-effectiveness threshold*. The threshold symbolizes a cut-off point or a *critical ratio*, as defined by Weinstein and Zeckhauser,[3] for allocating resources among competing uses in a budget-constrained environment.

There are multiple ways to establish the threshold value. There is substantial disagreement among authors on the most appropriate means for identifying the threshold and what value it should take.[4] Garber and Phelps[5] describe the threshold as essentially a value judgment that depends upon several factors, including who the decision-maker is, what the purpose of the analysis is, how health gains and costs are valued (and weighted), what risks are considered, and, finally, what resources are available. The answers to these factors essentially indicate the perspective considered while formulating the threshold; that is, which stakeholders' (patient/consumer, insurer, government) value for health and cost is reflected by the threshold. A consumer's threshold should reflect their willingness to pay, an insurer's threshold would reflect the market demand for the intervention, and a government's threshold should reflect the social value consensus, perhaps through a social welfare function.

The diverse ways in which a threshold can be estimated can affect how a decision-maker interprets them and hence uses them for decision-making. According to McCabe et al.,[6] a threshold can be defined in three potential ways: i) it could be inferred from previous decisions; ii) it could be defined to set an optimal healthcare budget; and iii) it could be set to exhaust an exogenously given budget.

The first method involves using benchmark interventions or previous decision rules to guide current decisions. This was originally proposed by Weinstein and Zeckhauser.[3] These thresholds emerge from retrospective analysis of an existing practice.[7] An example could be the threshold of US$50,000 per QALY gained, previously used in the United States (now increased to US$100,000 per QALY), which is believed to be based on the CEA of the dialysis for chronic renal failure.[8] The use of inferred thresholds may be convenient but, due to issues of unknown confounders, they may be too high or too low; that is, they may not adequately reflect either society's willingness-to-pay (WTP) or the opportunity costs of adopting the technology.

The second and third methods are popularly cited as the *demand-side* and *supply-side* approaches, respectively. The demand-side approach requires the society's WTP for health care to determine the threshold which would guide the healthcare budget accordingly. The marginal WTP can be elicited through several ways: i) using revealed/stated preference methods through a representative sample; ii) contingent valuation studies by using value of health/life employed in other areas of resource allocation; and iii) assuming the gross domestic product (GDP) per capita would reflect it.[6, 9] The latter approach has been heavily criticized for the implicit assumption that there is a fixed relationship between GDP and the appropriate magnitude of expenditure on health care, whereas

this is a policy decision that can legitimately vary in terms of whether there is a relationship and, if so, the form and magnitude of that relationship.

The WTP in general is hard to quantify and generalize, as individuals may attach different weights to benefits from health care depending upon the value they attach to health, the process of health care, the other economic activities that health is an input to, and their attitude to risk. Hence, forming a social WTP by aggregation can be both empirically complex and conceptually difficult to justify. In general, demand-side methods fail to reflect affordability of new technologies, and hence do not inform the real trade-offs that are at the center of health technology reimbursement decision-making.[8]

The supply-side method is conceptually related to the *cost-effectiveness league table* approach, wherein the interventions are ranked in increasing order of their ICERs, and funding decisions are made starting from the one with the lowest ICER moving upward until the budget is exhausted.[2] However, the league table approach does not necessarily throw light on other issues such as equity (size and characteristics of the affected population), ethical concerns (provision of life-saving drugs and treatments), and political feasibility.[6] It also assumes that that all interventions are ranked in correct order, are divisible, exhibit constant returns to scale, and are completely independent of each other. In the event of uncertainty, this method fails to deliver a first-best solution.[10] The empirical work of Claxton et al.[11] shows that, when we only assume a fixed budget, the displaced technologies are not necessarily the least productive ones; rather, they may be those that are managerially the most convenient in the short run to remove or reduce. In such a case, the threshold should reflect the ICER of the displaced technology, which will be a second-best solution and higher than the first-best.

## Changing value of threshold

In the supply-side model, it is important to note that the threshold is not constant but rather will change in response to a number of factors. Paulden et al.[12] present comparative static analyses that show how changes in budgets, demand for currently funded technologies, medical inflation, and pace of innovation will lead to changes in the supply-side cost-effectiveness threshold. The threshold can increase (decrease) with budget expansion (contraction), increasing (decreasing) demand of existing technologies and decreasing (increasing) effectiveness of existing technologies. The dynamic nature of the cost-effectiveness threshold needs to be born in mind when considering its use in a value-based pricing framework. Fixing the threshold value for a period of time requires the capacity compensating changes in budget to maintain the threshold or the actual impact of a value-based price may diverge from the intended objective.

## Budget impact

In determining a supply-side threshold, a candidate technology can have an impact on the budget that may result in displacement of one technology (marginal budget impact) or multiple technologies (large/non-marginal budget impact). This can have repercussions in empirical estimation of a supply-side threshold. The more technologies that get displaced, the lower the ICER threshold is going to be, such that the threshold will reflect a weighted average of the displaced technologies.[12]

A detailed discussion on effectiveness versus affordability is provided by Lomas et al.,[13] who have examined the opportunity cost of larger scale (non-marginal) budget impacts. They incorporated the non-marginal budget impacts while estimating the supply-side threshold and showed that, as theory predicted, the threshold is indeed lower than that found by Claxton et al.[11] This reiterates the

observation from Paulden et al. that a technology may be affordable (as in its budget impact is less than the total budget from which it will be funded), but not cost effective.[12]

## Summary

CEAs produce ICERs and an input to resource allocation decision processes. However, an ICER cannot be interpreted without a reference standard that differentiates good from poor value. This reference standard is called the *cost-effectiveness threshold*, and it is an empirical parameter for decision-makers that may be estimated either as the WTP for an additional unit of health benefit, when the healthcare budget is assumed to be unconstrained, or as the opportunity cost of adopting a technology at the margin of the healthcare budget, when the budget is assumed to be constrained. As healthcare budgets are increasingly recognized as being at least partially constrained, the latter definition – referred to as the *supply-side* model of the cost-effectiveness threshold – is broadly considered the appropriate form of the cost-effectiveness threshold to use in decision-making. In the context of the Patented Medicine Price Review Board (PMPRB), the supply-side cost-effectiveness threshold is an operationalization of the concept of an excessive price that defines a price as "excessive" if it displaces more benefit through opportunity cost than the technology produces.

The supply-side cost-effectiveness threshold can be estimated empirically, as has been demonstrated by Claxton and colleagues for a range of countries, using both QALYs and DALYs as the measure of value. The dynamic characteristics of the supply-side cost-effectiveness threshold are increasingly well understood, which allows the policy implications of any specific value-based pricing policy to be well understood. Given the advances in the theoretical and empirical evidence on the supply-side cost-effectiveness threshold, its use has the potential to add to the transparency of PMPRB processes, and is consistent with an evidence-based policy paradigm.

# SECTION 2: The relationship between demand- and supply-side cost-effectiveness thresholds

The cost-effectiveness threshold or the cut-off point used to make critical funding decisions in a budget-constrained environment can be conceptually viewed through two perspectives, as discussed in Section 1. The demand-side perspective encapsulates the society's WTP for health gains or avoiding health losses. The supply-side perspective, on the other hand, captures the opportunity cost that results from disinvestment to fund more cost-effective technologies.

The demand-side threshold ($v$) is determined by the willingness to contribute to the private health expenditure by individuals in a society. The WTP of every individual can be aggregated to ascertain this value or, in some cases, the collective WTP for the society's health can be evaluated as well. This value is therefore linked to the incomes and share of income devoted to health by individuals.

The supply-side threshold ($k$) is determined by the opportunity costs of disinvesting when new interventions need funding. Since this evaluation is done in a budget-constrained environment, the healthcare budget has a pivotal role in affecting this threshold value. The healthcare budget is a decision undertaken by the government in power, which should ideally reflect the preferences of the people that elected it. In that way, the individual's income again affects the threshold value through the contribution to tax revenue, which the government uses for funding various sectors of the economy.

## Linking the two sides conceptually

The demand-side considers the threshold as the WTP for health improvement by individuals or the consumption value of health. Using this definition, health becomes a consumption good for individuals, entering their utility function. The objective is, therefore, to maximize the utility over health and other consumer goods given the budget of individuals. This maximization exercise generates a demand for health as a consumption good if prices for health and other goods are given and income is exogenously determined. This "demand for health" is the threshold from the demand-side.

Factors affecting the demand-side threshold are:

- individual income;
- prices of health services;
- prices of substitutes and complementary goods to health; and
- environmental changes affecting the demand exogenously.

The supply-side considers the opportunity cost of the government budget spent on health, that is, the marginal productivity of the health care system, which can be visualized as an input in the health production function of the government.

The government or the public sector is believed to contribute to the total welfare of the individuals using investments in health care, education, infrastructure, et cetera as inputs. Health is therefore considered as an investment good from this side of the economy that can lead to higher income in the economy. Tax revenues are the income for the government in this model. The objective function for the government is assumed to be to maximize the net benefits (profit function) given

the input prices (for example, costs of health, education), or to minimize the costs of producing the government's total contribution to welfare given the tax revenue.

The outcome would be the optimum amount of health care that the government would generate/supply such that total welfare of individuals is maximized. This amount would reflect the marginal productivity of health care and will account for the competing uses of the government budget. Therefore, it reflects the supply-side cost-effectiveness threshold.

Factors affecting the supply-side threshold are:

- prices of healthcare technologies;
- prices/cost of providing other services by government;
- tax revenue collected by government; and
- technological developments in health sector.

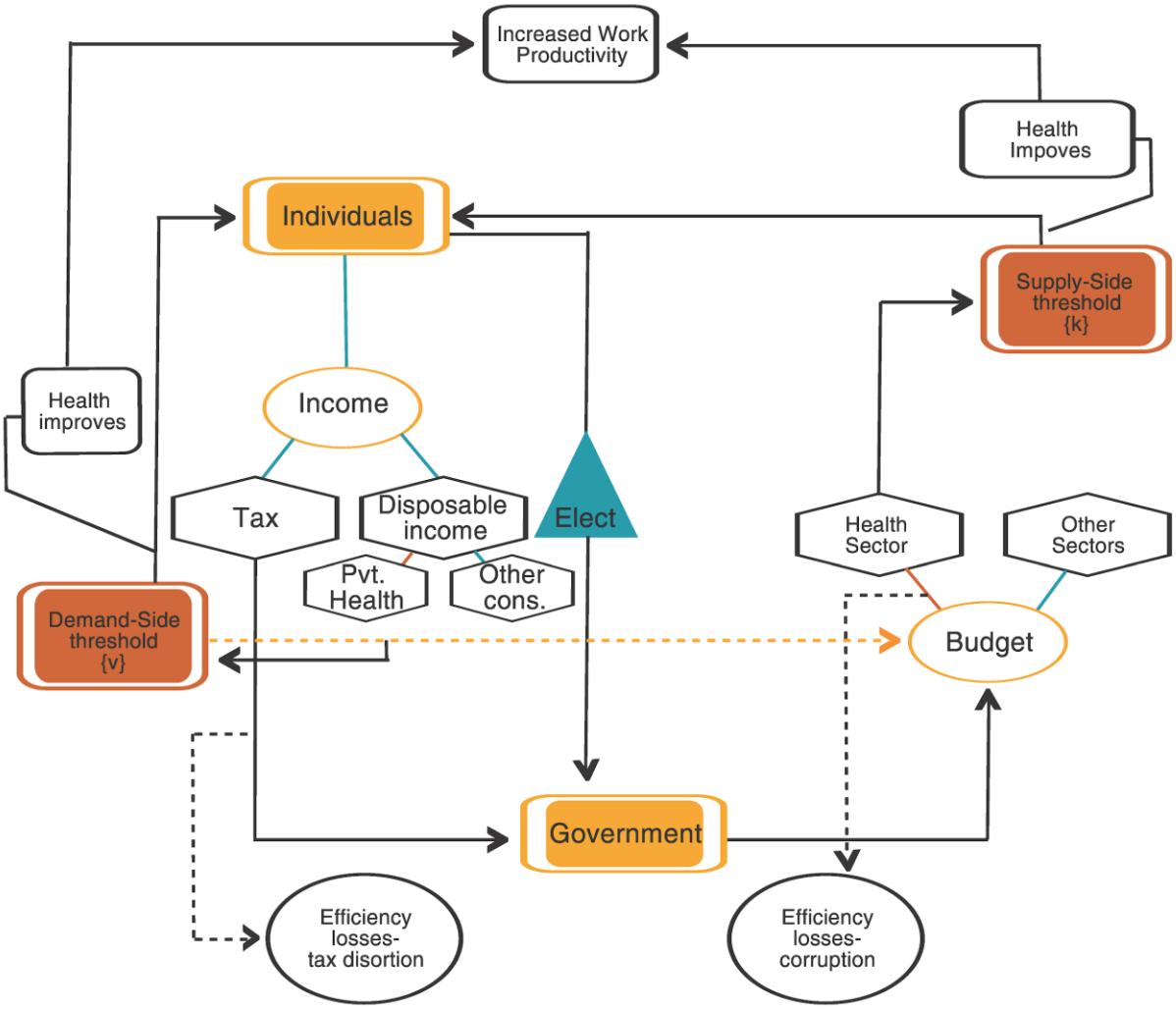
Factors affecting the demand-side and supply-side thresholds, as discussed above, are interrelated or common. Thus, both the measures can change simultaneously. The income base for individuals and the government play an important role in determining how the two measures are related.

## Link between *v* and *k*

It is often argued that for making funding decisions, the supply-side threshold (*k*) is what should be considered because it reflects opportunity costs. An estimate of the demand-side threshold (*v*), which reflects the consumption value of health or how much individuals are willing to pay for mortality reductions, *can* reflect the social value of health and thus inform decisions about scale of resources that should be allocated to the healthcare budget; *v* may therefore reflect the size of the healthcare budget.[10]

However, this link is dependent upon the decisions of government in fixing the healthcare budget. The government's capacity and willingness to reflect society's preferences for health in fixing its budget is a dimension of the political economy models. Further, government's scale of activities can impact the efficiency in health delivery, and therefore understanding the efficiency losses and gains of government activity is critical to determine the relationship between *k* and *v*. A conceptual model is outlined in Figure 1.

**FIGURE 1: The relationship between *v* and *k* cost-effectiveness thresholds**




## Conceptual background

Through a simple flow mechanism, the basic working of this threshold framework can be discussed. Under varied assumptions, the tax rate, share of contribution to private health (WTP for better health by individuals), and share of contribution to public health (government healthcare budget) are the main factors that can affect the threshold value.

The demand-side threshold (*v*) is determined through the amount individuals are willing to spend on private health out of their disposable income (income after paying taxes). The supply-side threshold (*k*) is determined through the amount government allocates towards health care out of the total budget (based on total tax revenues collected). Taxation appears to be an important factor on both sides of the estimation. Therefore, efficiency losses are important in determining both *v* and *k*. For *v*, there are losses due to distortionary taxes, while, for *k*, welfare losses occur due to misuse and misallocation of the tax revenues.

The role of the electoral system is crucial in this model. Individuals elect a government assuming the government would reflect on their preferences, and thus information flow plays an important role. The closer the government reflects the individual preferences of voters, the smaller the expected divergence between *v* and *k*, all things being equal.

## Alternative scenarios

### *When* v *and* k *are equal*

Both measures are believed to be equal only under the prevalence of strict assumptions of a hypothetical world where there is full information for individuals and the government regarding individual preferences, and the government has the capacity to act upon them. This would depend in part upon a transparent electoral system, an efficient health care system, and trust in the public sector. At the same time, all individuals must have homogeneous preferences such that the social-welfare function can truly reflect on the welfare of everyone. Under heterogeneity of preferences, it is likely impossible to aggregate individual preferences in a way considered socially legitimate, and hence any particular allocation of resources to health care (determining *k*) is unlikely to robustly align with the preferences of the majority of individuals (determining *v*).

### *When* v *and* k *differ*

The real world is far from this perfect scenario. There are informational constraints and often a society's preferences for health will not be reflected in the healthcare budget. In such a scenario, a political economy model reflecting the trust individuals place in their governments can throw light on this issue. If the individuals in a society have faith that the taxes paid by them are efficiently used up for providing for their health care and other services; and the level of satisfaction from the public health care system is high, then a demand-side threshold may be similar to the supply-side threshold. However, significant dissatisfaction with the public health care system will cause the demand-side threshold to be higher than the supply-side threshold, as those with the ability to pay purchase supplementary health insurance to meet their expectations.

It is likely that *v* is greater than *k* when the basic premise of trust in government is not strong enough. It can be routed in subtle ways through the welfare losses that occur due to the taxation system, and if the WTP of individuals is greater for themselves compared to that of the society in general. This creates uncertainty in the economy, and efficiency losses will increase as a result. It is worth noting that with efficiency losses in place, both due to deadweight losses in taxation and from the government's performance in allocating the budget, the value of *k* will need to be driven higher than the original *v* in order to compensate and match the social preferences. This is unlikely to be plausible with limited budgets.

Moreover, the value of *v* can be higher than *k* because the government operates with economies of scale. The value of *v* is affected by the coverage of the private insurance companies, and is therefore limited by the people insured in the economy either through employment or otherwise. The value of *k*, on the other hand, is governed by public insurance, which has a much wider coverage, potentially driving down the average administrative costs. The wider coverage can allow the government to provide various health technologies/drugs at a lower costs, due to greater negotiating power and economies of scale in associated clinical services compared to private providers, thus making it more cost-effective. This can have an effect of reducing the value of *k* per se. The extent to which this effect is observed in practice will depend heavily upon the degree to which government can realize the economies of scale and scope.

The other case of $k$ being greater than $v$ is plausible when the investment value of health is very high, and the individuals have high levels of certainty regarding the intentions of the government. Cuba is an example of this, where the government is highly committed to investment in health, thus making the individuals lower their own WTP for health care.

The ratio of $k$ and $v$ is also likely to differ across countries or within a country's provinces, owing to different income levels. Healthcare spending is assumed to have positive income elasticity with respect to incomes, and therefore higher income regions are expected to have higher healthcare budgets and greater spending. Also, in lower income countries, the size of the healthcare budget is likely to be constrained by the operational ability of countries to raise tax revenues.[15]

# Factors affecting the threshold

## Comparative statics

### *Assumptions*

- Individuals have homogeneous preferences.
- Income is exogenously determined.
- An increase in private or public health spending is assumed to have an equivalent effect in improving health.

Given the above assumptions, the threshold change is analyzed under different circumstances holding everything else static or constant.

### *Increase in tax rate*

Taxes play an important role in generating revenue for the government and thus in deciding the budget available for funding health interventions. At the same time, it also determines the income at the disposal of individuals. Therefore, the budget of both individuals and the government is affected through the tax rate. Under a static scenario with all else being equal, a change in tax rate can change both valuations of the threshold ($k$ and $v$). As the tax rate rises, and tax revenue for the government rises, then, all else being equal, the public allocation to health increases and the supply-side threshold ($k$) rises. At the same time, with a higher tax rate, and less disposable income with individuals, their WTP for health may fall if the health delivery system is believed to be efficient, and thus the demand-side threshold ($v$) would fall. The impact on total health expenditure remains ambiguous, as the direction of dominance between public and private health expenditure needs to be evaluated.

However, if government as discussed above is believed to have a wider coverage for healthcare provision and the private WTP is only affected by the availability of private insurance, which is limited in reach due to its availability to individuals with employment or higher income or risk averse nature, then a rise in $k$ could dominate the fall in $v$, thus causing total health expenditure and health in general to rise.

### *Increase in share of private expenditure on health*

The share of the contribution to health expenditure by individuals from their disposable income is key to determine their WTP for own health, thus deciding the value of $v$. A higher contribution to health expenditure by individuals, either due to greater private insurance or better employment benefits, would cause the value of $v$ to rise, all else being equal. This would be independent of the tax revenues, and so there would be no impact on the value of $k$. A higher $v$ with a constant $k$ would

unambiguously cause the total population health to improve, due to the increase in total health expenditure.

### *Increase in share of public revenues allocated to health care*

The government allocation of its budget to healthcare investment is an important determinant of *k*. All else being equal, with greater public spending on health, the individual WTP for health would either remain same or fall, thus causing *k* to rise with a lower or unchanged *v*. Total health expenditure would increase, again leading to improvement in total population health.

## Comparative dynamics

The analysis can be expanded to consider a dynamic situation, where the impact of a shock can be felt over multiple periods like a multiplier effect. Considering dynamic effects is important, as health improvements are linked to the earning capacity of individuals through their ability to work more efficiently with better health. Income therefore becomes endogenous to health, and we would expect a multiplier effect to be observed.

### *Assumptions*

- Income is endogenous to health levels.
- Expenditures in health, whether private or public, are positively related (linearly) to health outcomes.
- Individuals have homogeneous preferences.

All dynamic effects will be analyzed over two periods (which can easily be extended to further periods), modelling the effects as a chain reaction.

### *Increase in tax rate*

In the first period, a rising tax rate would cause the government budget to rise and the individual disposable income to fall. Thus, the value of *k* increases and value of *v* decreases. This would cause the private health expenditure to fall and the public health expenditure to rise. The impact on total health expenditure is the same as discussed in the *Comparative statics* section above. There is ambiguity in general; however, there are reasons to expect that health expenditure may rise if public expenditure dominates private expenditure, causing the total population health to improve.

Similarly, in the second period, if there is ambiguity then the further chain reaction cannot be ascertained without simplifying assumptions. If the government operates with economies of scale due to wider coverage of health care, then there would be an unambiguous rise in incomes with higher health expenditures. This would lead to higher *v* and higher taxes as well, which could convert to higher *k*. This would lead higher levels of health in all periods thereafter.

### *Increase in share of private expenditure on health*

In the first period, higher private expenditure on health would cause *v* to rise with a constant *k*. There would be an unambiguous rise in total health expenditure and total population health.

In the second period, this would cause the incomes of individuals to rise with enhanced work productivity, thus leading to rising taxes and contribution to private health. As a result, *k* and *v* would rise, causing total health expenditure and health levels in the society to increase in the periods thereafter, continuing the multiplier effects.

***Increase in public allocation on health***

In the first period, an increase in the government's healthcare budget will, all else being equal, lead to a rise in $k$ and a fall/no-change in $v$ (depending on the level of substitutability of private and public expenditure in health). Total health expenditure will rise, leading to a rise in health levels in society.

Thus, in the second period, with higher individual incomes, the multiplier effect can set in and the values of $k$ and $v$ can continue to rise to match social preferences and the budget, leading to higher levels of health.

## Summary

Having discussed the conceptual background to the possible links between demand- and supply-side thresholds ($v$ and $k$, respectively) with an outlook on how shocks such as changes in tax rate, private provision to health care, or public allocation to health care can impact the overall health levels in the economy in the short run as well as longer time periods, the various channels of threshold determination are understood. This working knowledge can be improved further by considering the political economy and allowing the relaxation of excessively simple assumptions, such as a linear relationship between health expenditures and health outcomes, and homogeneity in individual preferences. In the real world, we witness diminishing returns to health expenditures and thus non-linear relationships, which would reduce the multiplier effects eventually. Further, it is well known that individuals are heterogenous and their preferences can also vary with respect to their incomes and other factors.

In general, the potential for greater efficiency through economies of scale suggest that $k$ can be lower than $v$, while preference heterogeneity means we cannot conclude as to whether $v$ can be reliably identified and hence whether any specific value of $k$ is above or below the $v$ that would be observed if all health care was funded through private finance (either out-of-pocket or private insurance). The analysis presented in this section would suggest that, if decisions based on $k$ were substantially discrepant with individuals' values, there would be an increasing use of private insurance. As the proportion of Canadian health care that is privately funded has been stable at 30% since the year 2000, with around 12% of care being funded by private insurance, there is a prima facie case that $k$ is sufficiently close to $v$ for the majority of Canadians.

# SECTION 3: Empirical estimates of demand- and supply-side cost-effectiveness thresholds

As discussed elsewhere, a cost-effectiveness threshold can be conceptually understood through two approaches: i) how the society values health gains, or/and ii) the opportunity cost involved in displacement of another technology in the health care system.[16] The literature on the estimation of cost-effectiveness thresholds are therefore categorized widely into these two domains, also referred to as the *demand-side* and *supply-side*, respectively.

In order to conduct a critical review of the related literature, a systematic search was conducted using the key papers in this field as identified by Claxton et al.,[11] dating up until 2013. We performed a forward and backward search on those key initial papers, updating up until 2017, to find 67 related papers, including some very recent systematic reviews.* A recent review by Vallejo-Torres et al.[17] identified 38 studies, out of which 29 were classified as demand-side studies and the remaining nine as supply-side studies. Their review findings suggest that estimates based on the demand-side approach tend to be higher than the estimates based on the supply-side approach. This, according to the authors, could suggest that "some interventions with positive social net benefits, as informed by individuals' preferences, might not be an appropriate use of resources under current budget constraints."

The literature on threshold estimation through the demand-side includes a wide variety of studies that allow for eliciting social preferences on the threshold via an aggregated method of adding the ratios of WTP over QALY gains, or via a disaggregated method of computing a ratio from the sum of WTP and QALY gains for all individuals. The other kind of studies under this category include those which infer the threshold value using the value of a statistical life (VSL), which can be computed through contingent valuation studies or revealed/stated preference methods that are commonly used in transport- and environment-related policy studies.[18]

Demand-side threshold estimates that are based on WTP surveys include several studies such as Shiroiwa et al.,[19] who conducted an international survey on general health to find that the average WTP for an additional QALY at a disaggregated level varied significantly from country to country, from £23,000 in the United Kingdom to US$62,000 in the United States and NT$2.1 million in Taiwan. Baker et al.,[20] based on aggregation of individual preferences for headache in England, found a threshold in the range of £22,570 to £41,350. Bobinac et al.[21] found a threshold for general health in the Netherlands in the range €80,800 to €113,000, by aggregation of individual preferences. Martín-Fernández et al.[22] estimated a range of WTP thresholds in Spain through disaggregated pooling of individual preferences, using different methods to elicit the WTP.

The other segment of literature on the demand-side includes Hirth et al.,[23] who determined the value of a QALY as implied by the VSL literature and compared this value with arbitrary thresholds for cost-effectiveness that have come into normal use. They identified 42 estimates of the value-of-life that were appropriate for inclusion through a literature search. Donaldson et al.[18] addressed the issue of threshold in two ways, first by modelling it using the United Kingdom health value of prevented fatality from the transport department to arrive at values in the range of £10,000 to £70,000 per QALY, and second by conducting a survey to test the feasibility of combining respondents' WTP and health state utility regressions. Via the survey, most methods of aggregating resulted in threshold

* Some recent papers from 2017-2018 were also added manually to our search.

values in the range of £18,000 to £40,000. These contrasted with the threshold range used by the National Institute for Health and Care Excellence (NICE) of £20,000 to £30,000.

A more detailed review of the demand-side estimates can be seen in Vallejo-Torres et al.[17] The multiple studies on the demand-side show considerable variation in estimates for the threshold, which can be attributed to the difference in methods of aggregation of WTP as well as the methods to make QALY adjustments.[24] VSL-based studies, on the other hand, can have estimates higher than that of WTP-based studies, but they too show variations depending on the method chosen to value the end of life.

Although the literature is comprised of mainly demand-side studies, many authors consider that, in the presence of a constrained budget for health, the shadow price (or opportunity cost) approach is better suited to elicit the threshold.[11, 25]

The supply-side studies are fewer in number, as this approach is heavily dependent on a continuous availability of complete information on the costs and QALYs gained for all possible interventions in the health care system. Moreover, the opportunity costs estimation requires the know-how of exactly which activities sector-wise will be displaced when a new health technology needs to be funded.[26, 27]

The supply-side estimates therefore can be inferred from past funding decisions,[27, 28, 29] or through empirical estimation of the marginal cost of a QALY.[11, 30] Using past funding decisions to infer the threshold is conceptually weak, on the grounds that current decisions of decision-makers may not always correlate with past decisions, and there are always multiple factors that affect a decision-making process that need complete transparency to ascertain.

A summary description of recent supply-side estimates of the threshold is provided in Table 1.

Threshold evaluation studies based on estimates of opportunity costs in the health care system reflected by the cost per QALY are now picking up momentum. Some of the earlier ones include Lichtenberg,[31] who developed a health production function using time series data in the United States from 1960 to 2001 to estimate a threshold of $11,000 per life-year (LY). In Spain, Puig-Junoy and Merino-Castello[32] applied a similar methodology using health spending and life expectancy at birth from 1960 to 1997, and estimated a cost per LY less than €13,000. These studies could not provide robust estimates of $k$, as it is difficult to disentangle impacts of time trends in expenditure from other temporal influences in health.

Woods et al.[15] have exploited the relationship between the GDP per capita of a country and the VSL to compute the cost-effectiveness threshold for several countries, from the lowest of $3 (in Malawi) to the highest of $8,018 (in Kazakhstan).

The above-mentioned studies are constrained by limitations owing to endogeneity between incomes/expenditures and health outcomes. There have been some recent studies that have tried to (partially) address this issue by adjusting the estimated impact on mortality to account for health-related quality of life (HRQoL) to estimate the marginal cost of a QALY, and at the same time using more sophisticated methods for treating endogeneity issues with instrumental variables and panel data sets. For example, Martin et al.[33, 34] and Claxton et al.[11] measured the cost per QALY using administrative data for primary care trusts (PCTs) in England using the spending data. Martin et al.[33, 34] used data for 2005/06 for five specific diseases, while Claxton et al.,[11] using expenditure data for 2008/09, provided an estimate for each of the 23 disease programs and combined the disease-specific values to arrive at a central estimate of £12,936 per QALY.

Lomas et al.[13] have extended the analysis by Claxton et al.[11] using mortality as the outcome variable and expenditure data as the explanatory variable, aggregated for 23 programs of health care along with additional non-clinical groups. They have created separate subgroups for "under-target" and "over-target" PCTs to compare how the expected opportunity costs of proposed health investment varies across the subgroups, thus throwing greater light on the budget impacts. Subgroup-specific elasticities are computed and the resulting threshold value is slightly lower than the one computed by Claxton et al.,[11] at £12,452 per QALY. This indicates that health opportunity costs can be underestimated for bigger investments if scale of the budget impact is not considered.

Edney et al.[35] have computed an estimate of the average opportunity cost to fund new health technologies in Australia over 2011/12 using instrumental variable two-stage least square regression analysis accounting for issues of endogeneity. Adapting on the methods of Claxton et al.,[11] they have estimated a reference ICER of AU$28,033, adding to the nascent and evolving literature on empirical estimates of threshold from the supply-side. Vallejo-Torres et al.[30] have also computed a similar estimate for Spain, using a panel data set across 17 regional health services from 2008 to 2012. Even though they use fixed effects estimation to address endogeneity, an instrumental variable (IV) estimation is also performed to fully capture all sources of variation within regions and years that correlate with expenditure and health outcomes. Their estimate varies between 21,000€ and 24,000€.

## Summary

The literature on empirical estimates of cost-effectiveness thresholds across countries indicates that there are wide disparities in their values, owing to diverse assumptions placed in their estimation. Empirical estimates of thresholds differ not only with respect to the method of estimation (demand versus supply), but show variation also across different health care systems with different healthcare budgets. Demand-side thresholds are found to be on the higher end as of the current research, which can be explained to some extent through the theoretical underpinnings discussed in Section 2. It is still a nascent stage to comment on the exact linkages, as various assumptions used in empirical estimation need to be reevaluated. Linearity in the relation between health outcomes and expenditures is a core assumption of the supply-side analyses, which needs to be refined in the emerging research in this area. Since diminishing returns to health expenditures is theoretically established, it must be incorporated into empirical analysis as well. The decision to allocate scarce healthcare resources does need good supply-side threshold estimates, but, when the critical assumption of fixed budgets is relaxed, the support of demand-side thresholds is also relevant to throw light on the social preferences in deciding how to allocate any additional funds at the disposal of the health care system.

**TABLE 1: Summary of the studies estimating relationship between health expenditures and health outcomes**

| # | Title | Authors | Year | Method of estimation | QALY adjustment | Disease area | Country/ Region | Range of threshold |
|---|---|---|---|---|---|---|---|---|
| 1 | Sources of U.S Longevity increase, 1960-2001 | Lichtengber FR | 2004 | Time series: 1960-2001 | NA | Total expenditure | United States | $11,000 |
| 2 | Productividad marginal del gasto e innovacciones sanitarias | Puig-Junoy J, Merino Castelló A | 2004 | Time series: 1960-1997 | NA | Total expenditure | Spain | €9,329-€11,076 |
| 3 | Does health care spending improve health outcomes? Evidence from English programme budgeting data | Martin S, Rice N, Smith PC | 2008 | Instrumental variable | Utility scores by ICD-10 codes from HODaR project | Cancer, circulatory diseases | England | £19,070, £11,960 |
| 4 | Comparing costs and outcomes across programmes of health care | Martin S, Rice N, Smith P | 2012 | Instrumental variable | Utility scores by ICD-10 codes from HODaR project | Cardiovascular, respiratory, gastrointestinal, diabetes | England | £12,593, £13,256, £30,400, £47,069 |
| 5 | Methods for the estimation of the National Institute for Health and Care Excellence cost-effectiveness threshold | Claxton K, Martin S, Soares M, et al. | 2015 | Instrumental variable | Utility scores by ICD-10 codes from HODaR project | 23 program budget categories | England | £12,936 |
| 6 | Country-level cost-effectiveness thresholds: Initial estimates and need for further research | Woods B, Revill P, Sculpher M, Claxton K | 2016 | Income elasticities of VSL | NA | Overall | Malawi, Cambodia, El Salvador, Kazakhstan | $3-$116, $44-$518, $422-$1,967, $4,485-$8,018 |
| 7 | Estimating cost- | Vallejo-Torres L, | 2017 | Panel fixed effects - | Adjusted for | Total | Spain | €21,000-€24,000 |

| # | Title | Authors | Year | Method of estimation | QALY adjustment | Disease area | Country/ Region | Range of threshold |
|---|---|---|---|---|---|---|---|---|
| | effectiveness threshold for Spanish NHS | Garcia-Lorenzo B, Serrano-Aguillar P | | Instrumental variable | HRQoL by using EQ-5D weights | expenditure | | |
| 8 | Estimating the reference incremental cost-effectiveness ratio for the Australian health system | Edney LC, Haji Ali Afzali H, Cheng TC, Karnon J | 2017 | Instrumental variable - 2 SLS | Utility scores by SF-36 data and SF-6D algorithm | Total expenditure | Australia | AU$28,033 |
| 9 | Resolving the "cost-effectiveness but unaffordable" paradox: Estimating health opportunity costs to nonmarginal budget impacts | Lomas J, Claxton K, Martin S, Soares M | 2018 | Instrumental variable | Utility scores by ICD-10 codes from HODaR project | 23 program budget categories | England | £12,452 (non-marginal budget impact) |

# SECTION 4: Incorporating equity weights into consideration of value-based pricing: evidence and issues

The central tenet of value-based pricing is that the price paid should reflect the value of its health and resource impacts. In the context of the supply-side cost-effectiveness threshold model, this means that, when a technology has a positive budget impact, the value of the health care displaced to cover that budget impact must be less than the value of the additional health produced. In the context of the demand-side cost-effectiveness threshold, the value-based price is the price that produces an ICER that is exactly equal to the maximum WTP for health.[36, 37]

Many of the criticisms of value-based pricing are concerned with the specification of the value of the health produced.[38] Few, if any, health economists would argue that the value that individuals attach to health gains should be independent of the characteristics of the individuals to whom the gains accrue, or of the characteristics of the target health condition.[18, 39, 40] However, conceptual agreement on this point appears to be the limit of consensus in public debates regarding the "value" in value-based pricing. Paulden et al.,[41] reporting a scoping review of value arguments in the context of orphan drug reimbursement, identified 19 candidate determinants of value from 43 studies; the number of papers citing any one of these candidates ranged from one to 23.

Paulden et al.[41] also described a conceptual model for the incorporation of these broader measures of value into reimbursement decisions, within the supply-side threshold model. The implications of this model were elucidated further in subsequent publications. The central insight from this work is that, whatever definition of value is used to assess a technology, horizontal equity requires that the same definition is used to characterize the opportunity cost (value foregone to fund the additional cost of the new technology).

To recap, horizontal equity requires that "equals are treated equally," while vertical equity requires that "unequals are treated unequally." If a decision-maker chooses to value all health equally, irrespective of the characteristics of the individual who receives or loses it – frequently called the "QALY is a QALY" position[42, 43] –, this is a specific vertical equity position. Its advantage is that a decision-maker can apply this to the evaluation of a technology without having to know anything about the characteristics of the individuals who bear the opportunity cost of adopting that technology. A departure from this vertical equity position, for example to take account of the age of beneficiary of the technology (perhaps children or the elderly), complicates the decision-maker's task. They must know which patients bear the opportunity cost and hence to what degree the additional value applies, for example, how many children lose out. Failure to do this breaches the requirement for horizontal equity, as the decision-maker can no longer be confident that individuals with the same characteristics are being treated equally in their decision-making.[44, 45]

There is a small but growing body of empirical research on the values that societies should consider in healthcare reimbursement. Following on from McCabe et al.'s[46] call for empirical research on the question, in the context of evaluating ultra-orphan drugs, Desser and colleagues[47, 48, 49] produces a series of studies on the characteristics that might be taken into account, in a Norwegian context. These have been followed up with studies by Linley and Hughes in the United Kingdom,[50] and Shah et al.,[51] Rowen et al.,[52] and Chim et al.[53] in Australia. To date, the research overwhelming confirms that the greatest value is attached to the magnitude of the health gain. Many characteristics that have been argued for in the policy literature – such as prevalence and proximity to the end of life, and an "innovation" premium – have been consistently rejected. A small number of characteristics do

consistently receive support including the severity of illness: a) health gained by individuals with more severe illness being valued more highly than health gained by those with mild illness; b) treatments for illnesses for which there is no alternative therapy; and c) very high cost treatments, interpreted as treatments with catastrophic costs, that is, those that exceed the disposable income of the household.

Wailoo et al.[54] consider the question of the how evidence on the value of additional characteristics should be used by decision-makers. They observe that these additional characteristics would need to be incorporated into the value function, similar to the current utility algorithms that are used to calculate utilities from health state data. On this basis, they argue that the questions identified by Dolan[55] in the context of the measurement and valuation of health would still need to be considered. Hence, having established what is valued (for example, health plus the severity of the target condition and the [non-]existence of alternative therapies), decisions about whose value of these characteristics should be used (for example, general population or patients), how those values should be obtained (for example, standard gamble, time trade off, or discrete choice experiment), and how values for different combinations of these characteristics should be estimated (for example, linear additive or multiplicative functions) would have to be made. Some nine years later, there is no research that answers these questions. As Wailoo and colleagues discussed, given the current evidence, the application of empirical equity weights to inform value assessment will have to wait.

## Summary

While quantitative incorporation of equity considerations into cost-effectiveness analyses is not currently possible, the current evidence does support the incorporation of at least some additional value characteristics, in considerations of the value of new drugs. These considerations must of necessity be dealt with through qualitative consideration within the decision-making process. However, these considerations should be incorporated into the decision-making process in a way that is cognizant of the need to respect both horizontal and vertical equity.[10, 56]

# SECTION 5: Exposition of mechanisms for incorporating societal contribution to global pharmaceutical research and development into value-based pricing assessments

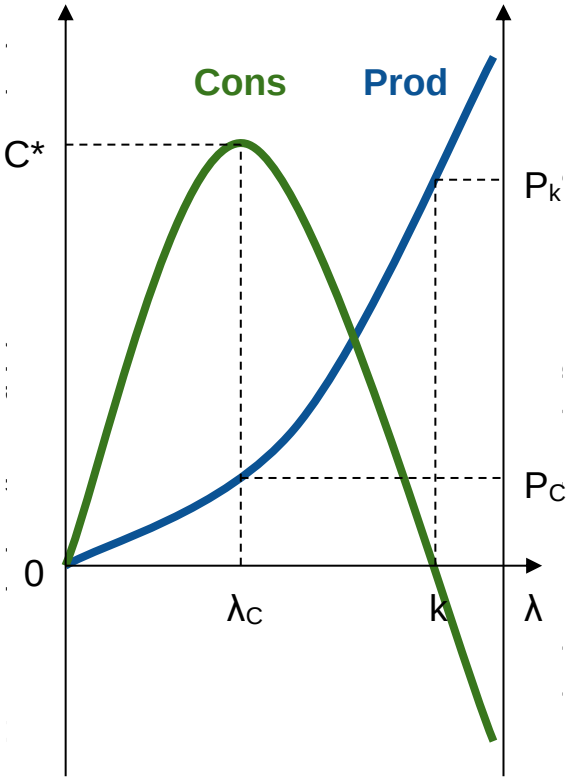
The existing supply- and demand-side approaches to estimating thresholds, as summarized in Section 3, do not take into account the allocation of consumer and producer surplus. Existing models also do not take into account strategic pricing behaviour on the part of manufacturers that might be expected to follow any specification of a threshold in practice.

The draft paper attached to this report proposes a new conceptual model of the threshold that incorporates both of these considerations. This model builds upon existing supply- and demand-side approaches to the threshold and integrates considerations from both. It reveals that the appropriate threshold depends upon a number of factors, including:

1. the conventional supply-side threshold (that is, the shadow price of the healthcare budget, and the subject of recent empirical work described in Section 3);
2. the conventional demand-side threshold (that is, the monetary value of a unit of benefit produced by the health care system, also the subject of empirical work);
3. the policy objective, specifically the desired allocation of the total surplus from the adoption of new technologies between consumers (patients) and producers (the manufacturers of new technologies adopted by the health care system); and
4. the distribution of reserve prices (and hence the distribution of reserve ICERs) for new technologies; this distribution reflects the minimum ICER at which manufacturers are willing to supply each new technology to the health care system, given the costs of production and the desire to make an acceptable return on the manufacturer's investment in research and development (R&D).

The attached draft paper describes in detail the assumptions made in the proposed model, and how the supply- and demand-side approaches can be integrated. The key findings from this draft paper are reproduced below in Figure 2 and Table 2.

**FIGURE 2: Consumer and producer threshold curves, reflecting the relationship between the threshold (λ), net population benefit (consumer surplus), and manufacturer profit (producer surplus)**




Where the objective is to maximize consumer surplus, the optimal threshold is $\lambda_C$. Note that $\lambda_C$ is lower than *k*, the conventional supply-side threshold, which in turn may be expected to be lower than *v*, the conventional demand-side threshold (see Section 2). Thus the proposed model finds that, under this objective, the specified threshold should be lower than that implied by both conventional approaches. If, in addition, there is a desire that producer surplus comprise a guaranteed proportion of the combined surplus, this may require that the threshold be increased above $\lambda_C$ but no higher than *k*, until this proportion is reached.

Where the objective is to maximize producer surplus, the optimal threshold is infinitely high. However, this results in negative consumer surplus; if there is also a desire for consumer surplus to be non-negative, then the optimal threshold is *k*. If, in addition, there is a desire that consumer surplus comprise a guaranteed proportion of the combined surplus, this may require that the threshold be lowered below *k* until this proportion is reached.

Finally, where the objective is to maximize the combined surplus, the optimal threshold lies somewhere above $\lambda_C$, with its precise location dependent upon the shape of each threshold curve and the conversion rate between consumer and producer surplus. If there is also a desire that both consumer and producer surplus be non-negative, the optimal threshold lies somewhere above $\lambda_C$, but no higher than *k*.

Based on recent empirical estimates of supply-side thresholds (£12,936, €24,870, and AU$28,033 per QALY in England, Spain, and Australia, respectively), the proposed model implies that, if decision-makers in these countries have a primary concern for maximizing consumer surplus, then thresholds lower than these should be specified in practice. The use of higher thresholds is consistent with an objective of maximizing producer surplus, subject to a weak concern for consumer surplus that serves only to limit the extent to which it is negative.

Specifying a threshold in Canada requires consideration of all of the factors described above. Particular attention should be paid to the policy objective. If Canadian decision-makers believe that new technologies should be adopted only if they provide positive consumer surplus, and if the assumptions of the proposed model are considered to be applicable (including strategic pricing on the part of manufacturers), then a threshold should be specified that is no higher than the shadow price of the healthcare budget, as estimated through a conventional supply-side approach. If there is a concern that consumer surplus be maximized, then a lower threshold should be adopted, but estimating precisely what this threshold is requires novel empirical research into the distribution of reserve ICERs across new technologies. Alternatively, if there is a concern that manufacturers receive a guaranteed proportion of the total surplus from new technologies, then a threshold somewhere between the two should be considered. This final concern might be borne out of a view that Canada should contribute a certain share towards global pharmaceutical R&D. It should, however, be considered that increases in the threshold to provide this share come at the expense of consumer surplus, that is, the benefit to patients derived from the health care system.

**TABLE 2: Optimal threshold (λ*) or range containing optimal threshold, for each objective**

| Policy objective | Optimal threshold or range containing optimal threshold | Comments |
|---|---|---|
| Maximize consumer surplus | $\lambda^* = \lambda_C$ | Consumer surplus is maximized by specifying a threshold of $\lambda_C$. |
| Maximize consumer surplus, subject to producer surplus comprising a guaranteed proportion of the combined surplus | $\lambda_C \leq \lambda^* \leq k$ | The proportion of the combined surplus allocated to producers increases above $\lambda_C$. If producer surplus comprises the required proportion at $\lambda_C$, then this is the optimal threshold. If not, the threshold should be progressively increased until the required proportion is achieved. |
| Maximize producer surplus | $\lambda^* = \infty$ | Producer surplus is maximized with an infinitely high threshold. |
| Maximize producer surplus, subject to consumer surplus being non-negative | $\lambda^* = k$ | Since producer surplus increases with the threshold, and consumer surplus is negative at any threshold above $k$, this objective is satisfied by specifying a threshold of $k$. |
| Maximize producer surplus, subject to consumer surplus comprising a guaranteed proportion of the combined surplus | $0 \leq \lambda^* \leq k$ | The maximum threshold at which each is non-negative is $k$. The optimal threshold is derived by progressively lowering the threshold from $k$ until the required proportion of consumer surplus is achieved. |
| Maximize the combined surplus | $\lambda_C < \lambda^* \leq \infty$ | Consumer and producer surplus both increase with the threshold up to $\lambda_C$. Above $\lambda_C$, consumer surplus falls and producer surplus increases. The optimal threshold depends upon the shape of each threshold curve but must exceed $\lambda_C$. |
| Maximize the combined surplus, subject to consumer surplus being non-negative | $\lambda_C < \lambda^* \leq k$ | Since consumer and producer surplus both increase with the threshold up to $\lambda_C$ but consumer surplus is negative above $k$, the optimal threshold must lie between $\lambda_C$ and $k$. |

# SECTION 6: Summary

In this report, we have described the relationship between demand- and supply-side approaches to the cost-effectiveness threshold, and have identified several reasons why the demand-side threshold might be higher than the supply-side threshold in practice.

In Section 3, we identified three distinct approaches for empirically estimating the cost-effectiveness threshold. We identified a number of estimates of willingness-to-pay (WTP) for health (demand-side) for different health care systems, and observed potentially important differences in the reported values according to the method used and the health care system context. A small number of studies reported indirect estimates of WTP based upon statistical analysis of observed funding decisions by healthcare payers. It is not possible to say whether these estimates are examples of a demand- or supply-side threshold, as decision-makers are not explicit about which model they are operating under. Further, these studies are subject to the concerns of unknown confounders that affect all observation analyses. A small number of studies reported supply-side estimates of the threshold. The United Kingdom estimates have used aggregate level data, but more recent estimates for Spain and Australia are based upon individual patient-level data. These supply-side estimates are consistently lower than published demand-side estimates and also conventional thresholds values assumed by decision-makers in the absence of empirical estimates. We did not identify empirical estimates of supply-side thresholds for Canada as a whole or for individual Canadian provinces.

In Section 4, we considered the incorporation of wider value considerations into cost-effectiveness-based health technology assessment processes. We identified a range of additional value characteristics being proposed by different authors. However, there was no clear consensus across authors about which of the many values should be considered. An emerging empirical evidence base was also identified on which value considerations matter to the general public. A societal preference for placing additional value on treatments for severe conditions, conditions for which there is no current therapy, and high cost/catastrophic cost treatments appeared to be consistent across studies. We identified a number of substantive challenges to quantitative approaches to incorporating wider value considerations into decision-making processes. First, there was a limited evidence base to support the choice of which wider value considerations to include. Second, there is even less evidence of the appropriate weight to attach to each consideration, relative to each other and to health outcomes. Finally, there is no evidence on the appropriate functional form for combining the value attached to health and each additional consideration. A further substantive challenge, specific to decisions operating under the supply-side threshold, relates to ensuring adherence with horizontal and vertical equity requirements. Unless decision-makers know the characteristics of the individuals who bear the opportunity cost of adopting a new technology due to its positive budget impact, as well as the characteristics of the beneficiaries of the new technology, a reimbursement decision based on wider value considerations may displace more highly-valued care than it produces; this is because the wider value characteristics may be more prevalent amongst those who bear the opportunity cost.

In Section 5, we reported a *de novo* conceptual model of the use of cost-effectiveness thresholds to make reimbursement decisions, examining a number of policy objectives regarding the distribution of consumer surplus (net population benefit for patients) and producer surplus (manufacturer profit). This novel framework is motivated from the observation that the cost-effectiveness threshold can operate as a signal to investors in developing innovative technologies, but is also subject to strategic pricing behaviour on the part of manufacturers. A summary of the findings of

this model was provided in the previous section, and a draft paper providing more detail is also attached to this report. The proposed model implies that the optimal threshold depends on the policy objective, and is generally lower than $k$ (the threshold from the conventional supply-side model) if improving consumer surplus is a policy concern. The model incorporates two threshold curves, reflecting the relationship between the threshold and consumer and producer surplus, respectively. The shape of the consumer threshold curve is influenced by strategic behaviour on the part of manufacturers. The share to society reflecting a target return on the societal investment in a) basic research and b) healthcare infrastructure is required to realize the value of the technology. Producer surplus provides a reward to manufacturers for their R&D in excess of the price that drives their reserve ICER, which incorporates their target return on R&D investment. The additional return on investment represents supra-normal profits, which act as a signal to other investors to enter into the market. Additional investors should, in principle, increase the probability of R&D investments leading to technologies that meet currently unmet needs.

The work presented in this report provides a number of key insights to inform policy debates around the move towards pharmaceutical price setting based upon cost-effectiveness thresholds: 1) demand-side thresholds will, except under unusual circumstances, be higher than supply-side thresholds; 2) there is a need for empirical research on both demand- and supply-side thresholds in the Canadian context; 3) wider value considerations, sometimes called *equity* or *ethical concerns*, must remain a qualitative process given the current evidence base – further research on which value considerations to include and how much value to attach to each (compared to health and each other) would be valuable; 4) specifying a threshold provides a mechanism for allocating the total surplus from new technologies between consumers and producers; and 5) where manufacturers strategically price to the threshold, specifying a cost-effectiveness threshold lower than $k$ is required if the adoption of new technologies is to increase consumer surplus – the supra-normal profits that arise from this behaviour also provide an incentive for R&D, particularly into technologies that may provide substantial benefit to the health care system at low cost, where the potential for supra-normal profits is maximized.

## Policy considerations

Value-based pricing has typically been used in reimbursement decision-making processes rather than a free-standing price setting activity. The use of the supply-side cost-effectiveness threshold to identify a maximum price for a technology is equivalent to defining an excessive price where the expected benefit displaced through its incremental cost is greater than the benefit the technology is expected to produce.

Identifying the cost-effectiveness threshold to be used in the price setting process can, conceptually, be undertaken using either a social WTP approach (the demand-side model) or a health benefit opportunity cost approach (the supply-side model). It is unlikely that the demand-side threshold ($v$) and the supply-side threshold ($k$) will be equal. Health care in Canada is, primarily, provided through publicly funded health care systems. There is increasing political pressure to bend the cost curve in Canadian health care, and professional organizations are advocating for clinical practice that promotes the financial sustainability of health care systems. In this policy context, it seems appropriate to design policy around the assumption that healthcare budgets are constrained, and hence the supply-side model is an appropriate framework for identifying the maximum cost-effectiveness threshold ($k$) for a value-based pricing policy.

The role of demand-side estimates of the WTP for health ($v$) is twofold. First, these estimates should inform the size of the healthcare budget; second, it can be used as the exchange rate between producer and consumer surplus, which would be essential if the threshold ($\lambda$) was to be set on the basis of sharing the total value produced by adopting new technologies between producers and consumers.

To identify the appropriate value of $\lambda$ to use in a value-based pricing policy, decision-makers need to be clear about the policy objectives, specifically about how the additional welfare created by innovative new technologies should be shared between producers (manufacturers) and consumers (healthcare payers). Setting $\lambda$ equal to $k$ is consistent with the objective of maximizing producer surplus, subject to the constraint that consumer surplus is non-negative. Maximizing consumer surplus from new technologies requires that $\lambda$ be set considerably lower than $k$. Values of $\lambda$ beyond $\lambda_C$ reduce the impact of new technologies on total population health benefit but may well be justified for equity reasons, for example, if the marginal technologies adopted address significant unmet needs or help otherwise disadvantaged members of society. When all manufacturers are able to price up to the threshold, the lost health benefit of setting $\lambda$ above $\lambda_C$ will be greater than if higher values of $\lambda$ are only applied to a subgroup of technologies that meet the equity criteria. There is an emerging empirical evidence base on societal preferences for equity considerations, which can be used to guide decision-makers' judgements. That said, the maturity of this evidence is not sufficient for the considerations to be included in quantitative analyses.

Values of $\lambda$ beyond $k$ are coherent with a policy objective that gives primacy to producer surplus, as they entail sacrificing current total population health in order to increase producer surplus. Values of $\lambda$ below all the expected reserve ICERs would mean that no new technologies will be available. The implication of this is that the health care system is not interested in improvements in efficiency through the adoption of new technologies.

The ability of decision-makers to make judgements about reserve ICERs, and hence the impact of any specific value of $\lambda$ on access to new therapies, is hampered by the information asymmetry between producers and payers with regard to R&D and the upstream and downstream cost of goods. While some legislators, particularly in the United States, are examining mandating the disclosure of R&D costs within price negotiations, this data is not typically accessible outside of the companies. In these circumstances, setting $\lambda$ at any specific level will reflect a searching function, whereby the responses of manufacturers provide indirect information on their reserve ICERs. However, this information is also subject to strategic behaviour by the manufacturers.

In summary, the current model of the supply-side cost-effectiveness threshold incorrectly suggests that total population health benefit is maximized by setting $\lambda$ equal to $k$. This condition actually maximizes producer surplus, subject to the constraint that consumer surplus is non-negative. Value-based pricing using the supply-side cost-effectiveness threshold is feasible as a mechanism for operationalizing the concept of an excessive price. It is also possible to incorporate equity considerations into such a framework. Empirical evidence on a) the value of $k$ for Canadian healthcare payers, b) the reserve prices and hence ICERs for Canadian pharmaceutical products, and c) the demand-side cost-effectiveness threshold (WTP for health) of Canadian citizens would significantly enrich the value of implementing this approach.

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# Appendix 1: Strategic Behaviour and the Cost-Effectiveness Threshold: A New Conceptual Model

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# Introduction

Many publicly funded health care systems use ‘health technology assessment’ (HTA) to inform decisions regarding which new technologies to fund. An important component of such assessments is a determination of which new technologies are “cost-effective”. This typically involves a comparison of the incremental cost-effectiveness ratio (ICER) of each new technology to a “cost-effectiveness threshold”.

Recent years have seen a number of advancements in our theoretical and empirical understanding of how the cost-effectiveness threshold should be specified (Vallejo-Torres et al. 2016; Paulden et al. 2017; Lomas et al. 2018). It is now broadly accepted that there are two conceptually different theoretical approaches to specifying such thresholds - often characterised as ‘supply-side’ and ‘demand-side’ approaches - and that the relevance of each depends upon the context in which decisions are made.

A conventional supply-side approach for specifying the threshold is widely considered to be appropriate for decisions regarding whether or not to adopt new health technologies into a health care system subject to a constrained budget, where the opportunity cost is expected to fall elsewhere within the same budget, and where the policy concern is to maximize some measure of ‘benefit’ across the population as a whole (Claxton et al. 2011). This ‘benefit’ is often assumed to be measurable in quality-adjusted life years (QALYs), although the implications of the supply-side model also hold if other measures of benefit are used instead.

By contrast, a conventional demand-side approach for specifying the threshold is considered to be appropriate where the opportunity cost of adopting new technologies is expected to fall upon individual consumption and the policy concern is whether or not the consumption value of any health gains exceeds the associated consumption loss.

Regardless of the approach taken, specifying thresholds in practice requires empirical evidence. Although empirical estimates of demand-side thresholds have been available for many decades, it is only over recent years that estimates of supply-side thresholds have been published (Vallejo-Torres et al. 2016). Recent empirical studies of public health care systems in England, Spain and Australia have reported base-case estimates of supply-side thresholds of £12,936, €24,870 and AU$28,033 per QALY, respectively (Claxton et al. 2015; Vallejo-Torres et al. 2017; Edney et al. 2017).

## The conventional supply-side approach

The recently published empirical estimates of supply-side thresholds reflect the relationship between marginal changes in health expenditure and health outcomes within each health care system. This relationship is frequently referred to as the 'shadow price' of the health care system budget constraint. For example, the AU$28,033 per QALY estimate from the recent Australian study represents the shadow price of the Australian health care system budget, reflecting the relationship between marginal health expenditures and health outcomes. This means that if expenditures on health care were to be increased by AU$28,033, all other things equal, we would expect one additional QALY to be produced. Conversely, if expenditures were to be reduced by AU$28,033 then we would expect one fewer QALY to be produced. Since, under the conventional supply-side model of the threshold, the health care budget is assumed to be constrained, every AU$28,033 spent on a *new* health technology would be expected to displace AU$28,033 from existing health care services, and hence would be expected to displace one QALY.

Proponents of a supply-side approach conventionally advocate for using this shadow price directly as the cost-effectiveness 'threshold' to which new technologies are compared. For example, if adopting a new technology would cost an additional AU$100,000 and provide two additional QALYs, then the technology's 'incremental cost-effectiveness ratio' (ICER) of AU$50,000 per QALY would be compared directly to the AU$28,033 estimate of the shadow price; since the ICER is higher than the shadow price, the technology would not be considered 'cost-effective'. If, instead, the technology provided 5 additional QALYs, then the ICER would be AU$20,000 per QALY; since this is lower than the shadow price, the technology would be considered cost-effective.

This conventional approach to specifying a supply-side threshold is consistent with a policy objective under which new technologies are considered cost-effective if, and *only if*, the benefits they provide exceed the benefits they displace. For example, if the shadow price is AU$28,033 per QALY, then a new technology that costs an additional AU$100,000 would be expected to displace approximately 3.6 QALYs. If the new technology provides more than 3.6 additional QALYs, its ICER will be lower than AU$28,033 per QALY and so it would be considered cost-effective. Conversely, if the technology provides fewer than 3.6 additional QALYs, its ICER will be higher than AU$28,033 per QALY and so it would *not* be considered cost-effective.

## Limitations of existing approaches

Many authors consider the conventional supply-side approach to be consistent with an objective of maximizing total benefits across the population (Claxton et al. 2011; Revill et al. 2015; Remme et al. 2017; Olsen 2017). However, this is mistaken for at least two reasons.

First, as Pekarsky has demonstrated, if the health care system is *inefficient* then there are at least two different 'shadow prices' to consider: the relationship between marginal *reductions* in expenditure and health outcomes associated with a contraction of existing health services through displacement (as considered in the conventional supply-side model), and the relationship between marginal *increases* in expenditure and health outcomes associated with a potential expansion of other health care services (Pekarsky 2012). In an efficient health care system these two shadow prices are identical, so estimating only one of these shadow prices is sufficient, but in an inefficient health care system these shadow prices will diverge, with potentially important policy implications. If the policy objective is simply to ensure that new technologies do not displace more benefits than they provide, then there is no need to estimate this second shadow price - policy makers need only compare the benefits from the new technology to the benefits forgone through the displacement of other health services (Paulden et al. 2014). However, if the objective is to maximize total benefits across the population, then both shadow prices must be considered (Eckermann & Pekarsky 2014). This is because the opportunity cost of adopting a new technology is not merely the benefits forgone through displacement, but also the forgone opportunity to use the resources freed up through displacement for the expansion of other (more efficient) health care services. The threshold to which new technologies must be compared in order to take this opportunity cost into account is lower than the first of these shadow prices, implying that a threshold set in accordance with the conventional supply-side approach would be too high.

Second, the use of any cost-effectiveness threshold in practice inevitably leads to strategic behaviour by the manufacturers of health technologies. This includes the practice of 'pricing to the threshold', under which a manufacturer will set the price of a new technology such that the ICER falls marginally below, but as close as possible to, the specified threshold. Alternatively, a manufacturer may initially price a technology such that the ICER is higher than the specified threshold, with the intention of later negotiating the price down with payers; the price may then be expected to fall through negotiations until the ICER reaches the threshold. Regardless of the mechanism used, there is clearly a strong incentive for each manufacturer to behave in a way that results in a final ICER (following pricing and negotiations) as close as possible to the specified threshold; if they did not, and the final ICER was substantially below the threshold, then the manufacturer would be unnecessarily foregoing potential profits. Under a conventional supply-side approach, where the threshold determined directly be the first shadow price described above, the result of this strategic pricing behaviour by manufacturers is that the expected benefits from new technologies are exactly offset by the benefits expected to be displaced. For example, if the threshold is set at AU$28,033 per QALY, and if manufacturers

price and/or negotiate such that the ICER for each new technology is as close as possible to AU$28,033 per QALY, then every additional AU$28,033 spent on a new technology will provide one QALY to the patients that benefit from the technology but will also forego one QALY among patients whose health care services are displaced; it follows that there is no *net* population benefit from adopting the new technology. If the policy objective is simply to ensure that new technologies do not displace more benefits than they provide, then the conventional supply-side approach to setting the threshold is consistent with this objective. However, if an alternative threshold exists at which net population benefits are positive, then the conventional supply-side approach is not consistent with an objective of maximizing total benefits across the population.

A further limitation of the conventional supply-side approach is that it considers only the benefits that arise to patients within the health care system. Under standard microeconomic theory, these benefits may be considered analogous to the 'consumer surplus' of the new technology. What is missing from conventional supply-side models is a consideration of 'producer surplus' - that is, profits to manufacturers arising from the adoption of new technologies.

The conventional demand-side approach also has important limitations. Not only does such an approach similarly ignore considerations of producer surplus, it also cannot be used to consider the consumer surplus arising from adopting new technologies within a budget constrained health care system; this is because a demand-side approach does not take into account any reductions in consumer surplus that result from the displacement of other health care services.

## The need for an alternative approach

If policy makers wish to ensure that new technologies provide positive consumer surplus in the presence of strategic behaviour on the part of manufacturers, or if they are concerned about the allocation of both consumer and producer surplus, it follows that an alternative approach for determining the appropriate cost-effectiveness threshold is required.

The purpose of this paper is to propose a new conceptual model of the cost-effectiveness threshold. This proposal incorporates conventional supply-side and demand-side considerations into a single model, and builds upon existing approaches by incorporating strategic behaviour on the part of the manufacturers of new technologies. The proposed model allows decision makers to consider how different specifications of the threshold might impact upon the distribution of consumer and producer surplus arising from the adoption of new technologies. It also illuminates some potential additional avenues for future empirical research in this space.

# Proposed model

The purpose of this section is to propose a new conceptual model of the threshold that accounts for two additional considerations:

1. Strategic pricing behaviour by the manufacturers of new technologies;

2. The impact of specifying a threshold upon ‘consumer’ and ‘producer’ surplus.

The proposed model is conceptual: it does not provide a ‘complete’ consideration of strategic behaviour or the determinants of consumer and producer surplus. Rather, the intention is to incorporate these considerations in a way that allows for consideration of potential departures from conventional approaches, while providing a framework to support future research.

After specifying some initial assumptions, the model will be developed first from the ‘consumer’ perspective (that of the health care system), and then from a ‘producer’ perspective (that of the manufacturers of new technologies supplied to the health care system). The models constructed under these two perspectives will then be combined. This will allow for consideration of the implications of specifying the threshold for the distribution of consumer and producer surplus. It will also allow for consideration of the ‘optimal threshold’ to use under each of a number of potential policy objectives.

## Assumptions

In common with the conventional supply-side model, we will assume that:

1. There is a publicly funded health care system with a constrained budget;
2. There is an accepted measure of the 'benefits' that patients derive from health care;
3. Adopting new technologies displaces existing health care services, resulting in forgone 'benefits' for other patients.

As in existing papers, we will refer to the shadow price estimated in the conventional supply-side model as $k$ (Claxton et al. 2011; Lomas et al. 2018). That is, $k$ represents the relationship between marginal reductions in expenditure on existing health care services and forgone benefits for other patients.

For clarity, we will refer to the threshold to which the ICERs of new technologies are compared as $\lambda$. This allows us to distinguish this threshold from $k$; while the conventional supply-side model assumes that $\lambda = k$, in our model these may differ.

In addition, we will make the following assumptions:

4. The threshold is publicly stated by a decision maker and held constant over some time period, during which numerous new technologies are appraised;
5. The manufacturers of new technologies are strategic and 'price to the threshold', resulting in ICERs equal to the threshold;
6. Each manufacturer has a minimum 'reserve price' that must be met before supplying each new technology - this price is sufficient to cover the costs of production and an acceptable return on the manufacturer's investment in research and development.

Each of assumptions 4-6 appears to be a reasonable approximation of real-world practice in many publicly funded health systems. For example, the UK's National Institute for Health and Care Excellence (NICE) has publicly stated that its baseline threshold is £20,000 - £30,000 per QALY; this has remained constant for many years, during which numerous new technologies have been appraised. There is also empirical evidence of manufacturers 'pricing to the threshold' (although it may be a simplification to suppose that manufacturers price *exactly* to the threshold, as assumed here). In Canada, there are established processes for manufacturers and payers to negotiate on price following assessment of the cost-effectiveness evidence, allowing for manufacturers to set a high initial price and then negotiate the price down afterwards; the use of 'risk-sharing' schemes in the UK and elsewhere provides another mechanism by which a high initial ICER may effectively be negotiated down to the threshold. Furthermore, it is reasonable to expect a manufacturer to refuse to supply a technology if the price is too low to meet its production costs and achieve an acceptable return on its investment.

For any given ‘reserve price’ for a technology, there is an associated reserve ICER. This is because the price is a factor in determining the incremental cost of the technology, and in turn the ICER. Typically, a reduction in the price will lower the ICER (all other things equal), while an increase in the price will raise the ICER; it follows that if the technology will not be supplied below a specific ‘reserve price’, then, equivalently, it will not be supplied if the ICER is below a specific reserve ICER.

The precise relationship between the ‘reserve price’ and reserve ICER for a technology may be complicated, since (i) the ICER depends upon the incremental cost, which in turn depends on more than just the price of the technology, and also (ii) the price and other components of the incremental cost may be incurred across multiple years and be subject to discounting. However, for the purposes of this model, it is not necessary to understand this relationship in detail. Rather, we only need to make the following assumption:

8. There is a distribution of ‘reserve prices’ across new technologies, which gives rise to a distribution of reserve ICERs. Each new technology will be supplied to the health care system if, and only if, the specified threshold exceeds the reserve ICER.

Finally, we will assume that the distribution of reserve ICERs is broad, with some lying below $k$ and others lying above $k$. This appears to be a reasonable assumption: violating this under a conventional supply-side approach (where $\lambda = k$) would result in *all* new technologies being adopted (if the distribution lies entirely below $k$) or *all* new technologies being rejected (if the distribution lies entirely above $k$), a clear departure from what is seen in practice. For simplicity, we will also not consider new technologies with zero or negative reserve ICERs, although very low reserve ICERs (close to zero) are permitted. Specifically, we will assume that:

9. ‘Reserve ICERs’ are continually distributed between zero and an ICER greater than $k$.

# Consumer perspective

From the consumer perspective, the outcome of interest is assumed to be the ‘benefit’ provided by the adoption of new technologies. Since adopting a new technology provides direct ‘benefit’ to some patients, but also results in the displacement of other health services and so foregone ‘benefit’ for other patients, it is necessary to consider the impact on *net population ‘benefit’*.

Net population ‘benefit’ is considered to represent the ‘consumer surplus’ that arises from the adoption of new technologies. Note that no assumptions are made regarding the ‘units’ used to measure this ‘benefit’. In practice, the QALY is frequently used for this purpose, but this is not required for the implications of the proposed model to hold. For the remainder of this paper, we will refer to a generic measure of net population ‘benefit’, rather than any specific measure.

## The consumer threshold curve

**Figure 1** plots what we will hereafter refer to as the “consumer ‘threshold curve’” (or ‘CTC’). This ‘threshold curve’ represents the relationship between the threshold used to determine whether a technology is ‘cost-effective’ ($\lambda$), represented on the horizontal axis, and the net population ‘benefit’ (consumer surplus) derived from the adoption of new technologies, represented on the vertical axis.

Note that the curve plotted here represents a *stylized* CTC that satisfies the basic properties described below. Understanding the exact *shape* of the CTC in practice requires empirical research into the distribution of reserve ICERs across all new technologies; this, in turn, depends upon the health care system in question and is beyond the scope of this paper. The aim of this paper is simply to outline the *properties* that we would expect the CTC to have and some of the resulting implications.

### Properties of the consumer’s threshold curve

The CTC bears some resemblance to the well-known ‘Laffer curve’, which describes the relationship between a tax rate and the resulting tax revenue (Fullerton 2016). The Laffer curve is anchored around two extreme points: a tax rate of 0% and a tax rate of 100%. At both of these anchor points the tax revenue is assumed to be zero. Between these points, tax revenue first increases and then decreases, such that there is some tax rate at which revenue is maximized. Although there is controversy around the *shape* of the Laffer curve and the point at which revenue is maximized in practice, the theoretical model nevertheless provides a useful insight: there is a tax rate above which revenues begin to fall, and so the optimal tax rate cannot be greater than this (Laffer 2004).

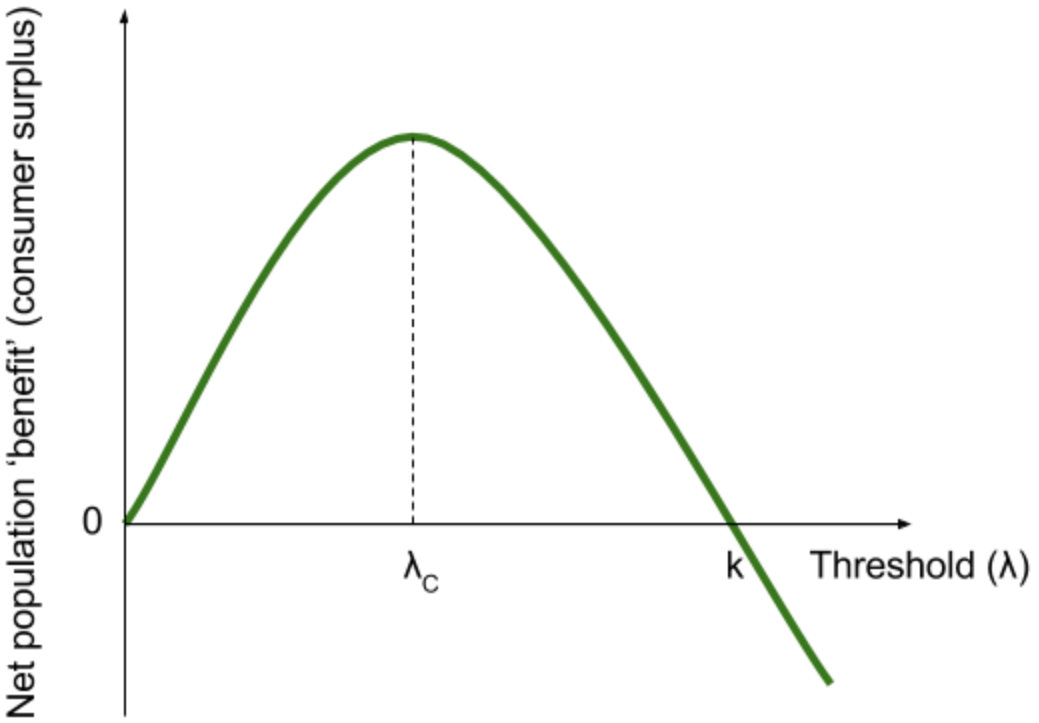


**Figure 1: The 'consumer threshold curve', reflecting the relationship between the threshold (λ) and net population 'benefit' (consumer surplus)**

The two anchor points of the consumer's 'threshold curve'

Similar to the Laffer curve, the CTC is anchored around two points on the horizontal axis: a threshold of zero and a threshold of $k$. Net population 'benefit' is zero at these anchor points. The reason for this is as follows:

- If the threshold is set equal to zero ($\lambda = 0$), no new technologies will be adopted. This is because the distribution of reserve ICERs lies entirely above zero (and hence $\lambda$), so the reserve ICER will not be met for any new technology. Since no new technologies will be adopted, it follows that no 'benefit' will be provided to patients, but also no 'benefit' will be displaced in other patients, such that the *net population 'benefit'* will be zero.

- If the threshold is set equal to $k$ ($\lambda = k$), then some (but not all) new technologies will be adopted. This is because some new technologies have a reserve ICER below $k$, such that manufacturers will be prepared to supply these to the health care system, while other new technologies have a reserve ICER above $k$ and so will not be supplied by manufacturers. For those new technologies that are supplied, some will have a lower

reserve ICER than others; however, since all manufacturers strategically 'price to the threshold', the actual ICER for each supplied technology will equal $k$. Adopting these technologies will result in one unit of 'benefit' being displaced for every unit of 'benefit' provided, such that the *net population 'benefit'* will be zero.

In common with the Laffer curve, the CTC begins from one anchor point, rises to a peak, and then falls to the second anchor point. However, unlike the Laffer curve, which is constrained between these two anchor points, the CTC intersects the horizontal axis at its second anchor point ($\lambda = k$) and extends beyond this point, becoming more negative with further increases in the threshold. The reasons for this particular shape are described below.

### The shape between the anchor points

The shape of the CTC between the anchor points results from two countervailing effects that arise from changes in the threshold. These may be examined by considering a marginal increase in the threshold from $\lambda_1$ to $\lambda_2$, where both lie between zero and $k$ ($0 < \lambda_1 < \lambda_2 < k$); this gives rise to the following effects:

1. The reserve ICER is now met for the subset of new technologies with reserve ICERs *between* $\lambda_1$ and $\lambda_2$. Previously these new technologies would not have been supplied by manufacturers, but following the marginal increase in the threshold these will now be provided. Since manufacturers strategically 'price to the threshold', each of these new technologies will be priced so that its ICER is equal to $\lambda_2$. Since $\lambda_2 < k$, the 'benefit' provided by each of these new technologies will exceed the 'benefit' forgone through the displacement of other health care services. This *additional supply* of new technologies therefore *increases* net population 'benefit'.

2. Manufacturers of the subset of new technologies with reserve ICERs *below* $\lambda_1$, which would have been supplied even prior to the increase in the threshold, will strategically raise their prices until the ICER for each new technology equals $\lambda_2$. This increases the 'benefit' forgone through displacement, without providing any additional 'benefit' to patients. This *strategic pricing* therefore *decreases* net population 'benefit'.

Between these anchor points, whether the CTC rises or falls following a marginal increase in the threshold depends upon the magnitude of each of these effects. If the first effect outweighs the second then the CTC will rise; if the second effect outweighs the first then the CTC will fall.

At the first anchor point ($\lambda = 0$), the first effect will be positive because a marginal increase in the threshold will cause a some new technologies to be supplied (those with very low reserve ICERs, such as some generics and other technologies with low marginal costs of production). The second effect will be zero because no new technologies have a reserve ICER below zero; since no new technologies are adopted when $\lambda = 0$, a marginal increase in the threshold from

the first anchor point does not result in any strategic price increases. It follows that the first effect outweighs the second effect, causing the CTC to *rise* from the first anchor point.

With each successive marginal increase in the threshold, the positive impact of the first effect will tend to *diminish* because the additional new technologies supplied will be priced up to a progressively higher threshold, resulting in a relatively larger amount of forgone 'benefit' through displacement and hence a smaller increase in net population 'benefit'. Meanwhile the negative impact of the second effect will tend to *grow* with increases in the threshold because the subset of new technologies with a reserve ICER below the threshold will also increase; with each successive marginal increase in the threshold, this growing subset of new technologies will be strategically priced up to the higher threshold, causing a greater amount of forgone 'benefit'.

As a result of the diminishing impact of the first effect and the growing impact of the second effect, a threshold will be eventually be reached where the magnitude of these effects is equal. At this threshold, the gain in net population 'benefit' that arises from a marginal increase in the threshold (due to an increase in the supply of new technologies) is exactly offset by the loss in net population 'benefit' due to strategic pricing from manufacturers. Since the CTC is neither rising nor falling at this point, this represents the *peak* of the CTC. The threshold corresponding to this peak is hereafter referred to as the 'optimal consumer threshold' and denoted as $\lambda_C$. Net population 'benefit' (consumer surplus) is maximized at this threshold.

Further marginal increases in the threshold beyond $\lambda_C$ result in a *reduction* in net population 'benefit', since the second effect now outweighs the first. Eventually, if the threshold is increased all the way to the second anchor point ($\lambda = k$), net population 'benefit' will reduce to zero and the CTC will intersect the horizontal axis. Net population 'benefit' is zero at the second anchor point because manufacturers will price new technologies so that each ICER equals $k$; as noted earlier, this will result in every unit of 'benefit' produced by new technologies being exactly offset by a unit of 'benefit' forgone by other patients due to displacement.

### The shape beyond the second anchor point

When the threshold is increased beyond the second anchor point ($\lambda > k$), the first of the two countervailing effects described above begins to impact upon net population 'benefit' in the *opposite* direction, such that *both* effects now act to *diminish* net population 'benefit'.

This is because each additional new technology supplied following a marginal increase in the threshold will be strategically priced to have an ICER above $k$, such that adoption will cause more 'benefit' to be forgone through displacement than will be gained by patients. As before, a marginal increase in the threshold will also cause the manufacturers of new technologies that would have been supplied at the previous threshold to price up to the higher threshold, causing additional displacement. It follows that increases in the threshold beyond $k$ will unambiguously cause net population 'benefit' to *fall*.

## Further considerations

The specific curve plotted in **Figure 1** is just one of a set of possible curves that satisfy the properties above. In practice, the shape of the CTC might differ from that in **Figure 1** for one or more reasons, including (but not limited to) the following:

1. The *skewness* of the distribution of reserve ICERs for new technologies. If a greater proportion of new technologies have very low reserve ICERs, then we might expect the peak of the CTC to be shifted to the left, resulting in a lower optimal consumer threshold. Conversely, if a greater proportion of new technologies have very high reserve ICERs, then the peak might be shifted to the right, resulting in a higher optimal consumer threshold. Nevertheless, regardless of the distribution of reserve ICERs, the properties of the CTC require that the optimal consumer threshold lies between zero and $k$.

2. The *density* of the distribution of reserve ICERs for new technologies. For any given threshold, the greater the density of the distribution of reserve ICERs below this threshold, the greater the number of new technologies adopted and the greater the *magnitude* of the gain or loss in net population benefit. This will cause a vertical stretch of the CTC in the vertical plane, but will not impact upon the location of the peak along the horizontal axis, and hence will not affect the optimal consumer threshold.

3. The magnitude of the *'benefit'* provided by adopted new technologies. Among new technologies with the same ICER, some may provide greater 'benefit', at a correspondingly higher price, than other new technologies. Adopting new technologies which provide greater 'benefit' will have a greater impact on net population 'benefit' than adopting new technologies with identical ICERs but which provide lower 'benefit'.

## Producer perspective

From the producer perspective, the outcome of interest is the profit provided to manufacturers by the adoption of new technologies. For the purposes of this model, it will be assumed that 'producer surplus' reflects the profits that arise to manufacturers that supply new technologies to the health care system.[1]

It should be noted that this definition of 'producer surplus' does not consider losses incurred by manufacturers of new technologies which are *not* supplied to the health care system. Since this is a potentially controversial assumption, a justification is provided below. A modified model which considers the implications of modifying this assumption is provided in the Appendix.

### Justification for excluding manufacturers who do *not* supply new technologies to the health care system

Supplying the health care system with new technologies is a competitive process. When a cost-effectiveness threshold is used to determine which new technologies are adopted and which are not, it is inevitable that some manufacturers will lose out. Where manufacturers have invested in research and development of new technologies, they may incur losses as a result.

When considering the impact of the threshold upon consumer and producer surplus, there are good reasons why an agency may wish to consider, when calculating producer surplus, *only* the profits arising to manufacturers who supply the health care system with new technologies, and not the losses incurred by *non-supplying* manufacturers. Considering these losses would serve to lower the overall producer surplus. In cases where the agency desires that a specific share of the overall surplus be allocated to producers, or adopts a constraint that producer surplus cannot be negative, it follows that considering losses incurred by *non-supplying* manufacturers may require an *increase* in the threshold to satisfy such an objective. This, in turn, will cause a reduction in net population 'benefit' (consumer surplus) if the threshold is raised above $\lambda_C$.

It is questionable whether the agency responsible for specifying the cost-effectiveness threshold has any obligation to diminish net population 'benefit' (consumer surplus) in order to support manufacturers who have failed to develop new technologies that provide additional 'benefit' to the health care system. It may instead be considered preferable to foster competition between manufacturers to supply new technologies at ICERs below the desired threshold. Those manufacturers who invest productively and manufacture new technologies efficiently will tend to have lower reserve ICERs than those manufacturers who are wasteful in their research and

[1] It is assumed here, for simplification, that each new technology is supplied by a different 'manufacturer'. In practice, a single manufacturer may supply multiple new technologies to the health care system, and may develop several other new technologies that are *not* supplied to the health care system. In this case, the 'producer surplus' considered in this model would reflect the profits associated with *only* those new technologies that each manufacturer supplies to the health care system.

development, adopt inefficient manufacturing techniques, or require unrealistically high rates of return before supplying their technologies to the health care system. Under the model proposed in this paper, the most efficient manufacturers - those who develop new technologies with the lowest reserve ICERs - receive *super-normal* profits when they supply their new technologies to the health care system, since they can strategically price up to the threshold. This provides a clear incentive for manufacturers to improve efficiency and develop new technologies that provide as large a 'benefit' to the health care system as possible at as low a cost as possible, both factors that will contribute to lowering the reserve ICER. Those manufacturers who are slightly less efficient, and develop new technologies with slightly higher reserve ICERs, will receive *smaller* but still *super-normal* profits when they strategically price to the threshold. Manufacturers with reserve ICERs equal to the threshold will make no super-normal profits, but also no losses. Losses will be incurred only by those manufacturers who are the least efficient at producing 'benefit' for the health care system, since their technologies will have reserve ICERs above the specified threshold and so will not be adopted.

Incorporating the losses incurred by *non-supplying* manufacturers into the consideration of producer surplus, resulting in a higher threshold, would diminish the incentives described above. Manufacturers who fail to develop new technologies that provide additional 'benefit' to the health care system may nevertheless be rewarded if the threshold is increased as a result of considering these losses. In addition, since manufacturers will now price up to a higher threshold, much of the gain in producer surplus will be enjoyed by manufacturers who would have supplied their technologies under the existing threshold; increasing the threshold serves to increase the already super-normal profits enjoyed by these manufacturers. Furthermore, manufacturers with reserve ICERs above the increased threshold will still incur the same losses as before.

It follows that raising the threshold is not necessarily an effective or efficient means of mitigating the losses incurred by manufacturers whose new technologies are *not* adopted by the health care system, are diminishes the incentives for manufacturers to efficiently develop new technologies that provide 'benefit' to the health care system. Limiting the consideration of producer surplus to *only* the profits enjoyed by manufacturers who *supply* new technologies to the health care system avoids these issues and encourages greater competition among manufacturers in the market to provide new technologies to the health care system.

## The producer threshold curve

**Figure 2** plots what we will hereafter refer to as the "producer 'threshold curve'" (or 'PTC'). This 'threshold curve' represents the relationship between $\lambda$, represented on the horizontal axis, and 'manufacturer profit' (producer surplus) arising from the supply of new technologies, represented on the vertical axis.

As with the CTC in **Figure 1**, the curve plotted in **Figure 2** represents a *stylized* PTC that satisfies the basic properties described below. Understanding the exact *shape* of the PTC in practice requires empirical research into the distribution of reserve ICERs across all new technologies. The aim of this paper is simply to outline the *properties* that we would expect the PTC to have and some of the resulting implications.

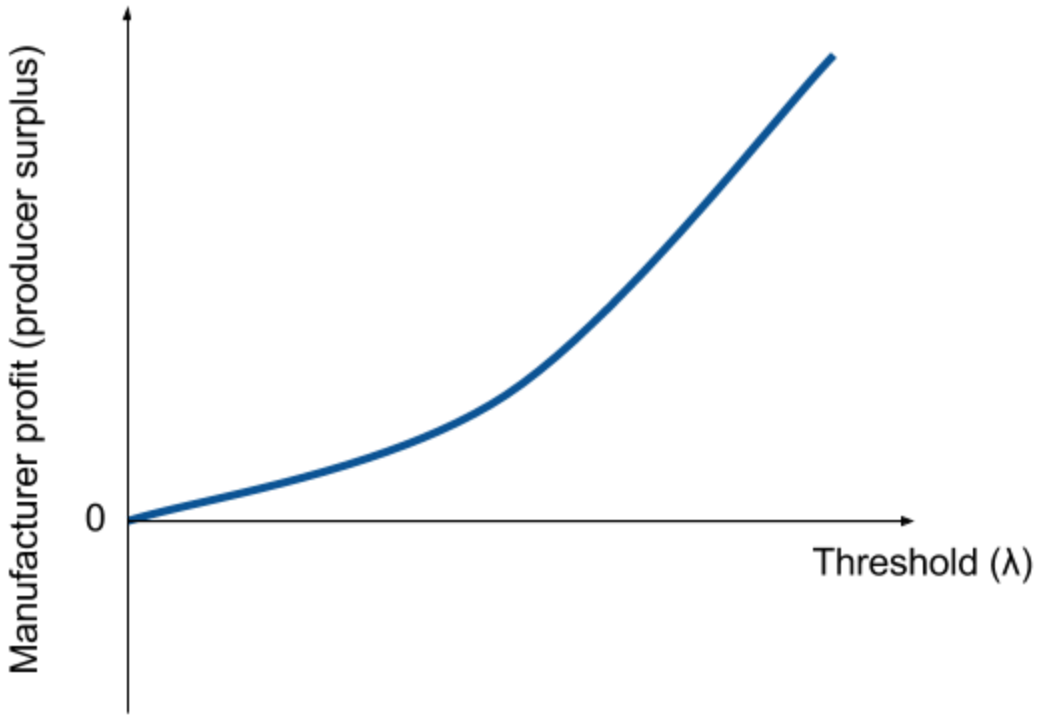


**Figure 2: The 'producer threshold curve', reflecting the relationship between the threshold (λ) and manufacturer profit (producer surplus)**

### Properties of the producer's 'threshold curve'

The PTC has the following properties:

- If the threshold is set equal to zero ($\lambda = 0$), manufacturer profit is also *zero*. This is because no new technologies are adopted by the health care system, and hence no manufacturers profit from supplying new technologies to the health care system.

- As the threshold increases above zero, manufacturer profit becomes *positive*. This is because new technologies with reserve ICERs below the threshold are now supplied to the health care system. Manufacturers of these new technologies strategically price up the threshold, resulting in *super-normal* profits.

- With further increases in the threshold, manufacturer profit will *unambiguously and continuously increase*. This is due to two effects, both of which cause profit to increase with the threshold. First, the reserve ICERs will be met for additional new technologies, causing them to be supplied to the health care system; each is strategically priced up to the threshold, resulting in super-normal profits for their manufacturers. Second, all new technologies with lower reserve ICERs (those that would be supplied even without an increase in the threshold) will now be strategically priced up to the higher threshold, resulting in additional profit for manufacturers.

It follows that the PTC lies entirely above the horizontal axis and continues to increase (without limit) with increases in the threshold. Even if the threshold is already so high that the reserve ICER is met for *all* new technologies, additional increases in the threshold will increase profits by allowing all manufacturers to price up to a higher threshold.

# Combining the consumer and producer perspectives

We will now combine the ‘consumer’ and ‘producer’ perspectives that were considered over previous sections. This will allow for consideration of the distribution of ‘consumer surplus’ and ‘producer surplus’ that arises under different specifications of the threshold. This, in turn, will allow for consideration of the ‘optimal threshold’ to adopt under different policy objectives.

## Converting ‘benefit’ and ‘profit’ into a common metric

Unless the measure of ‘benefit’ from the consumer perspective is already specified in monetary terms, a requirement for aggregating consumer and producer surplus is to convert each into a common metric. Whether this is done by converting consumer surplus into monetary terms or by converting producer surplus into units of consumer ‘benefit’ is immaterial; the most important and challenging task is identifying the relevant *conversion rate*.

A conventional *demand-side* approach to determining the threshold provides a natural source for such a conversion rate. Demand-side approaches typically involve estimation of the *monetary value* of a unit of ‘benefit’; such estimates may be used directly to convert net population ‘benefit’ into monetary terms, or to convert manufacturer profit into units of ‘benefit’, allowing both to be considered in a common metric.

Because there are competing methodologies for empirically estimating demand-side thresholds, and since any estimate is context dependent, for the purposes of this paper we will not assume any particular conversion rate between consumer and producer surplus. We will therefore constrain our consideration of the implications of our model to those which arise regardless of the conversion rate used.

## Comparing the consumer and producer threshold curves

**Figure 3** plots the CTC and PTC from **Figure 1** and **Figure 2** respectively on a single graph. This figure reveals the inherent tension between consumer and producer interests in any specification of the threshold. Setting the threshold equal to the ‘optimal consumer threshold’ ($\lambda_C$) maximizes consumer surplus, with a net population ‘benefit’ of C*. At this threshold, producer surplus is positive, with a manufacturer profit of $P_C$, but is not maximized; producer surplus can be expanded by increasing the threshold, but this comes at the expense of diminished consumer surplus. If the threshold is increased to $k$ then producer surplus rises to $P_k$ but consumer surplus falls to zero. At higher thresholds, producer surplus increases further but consumer surplus becomes negative.

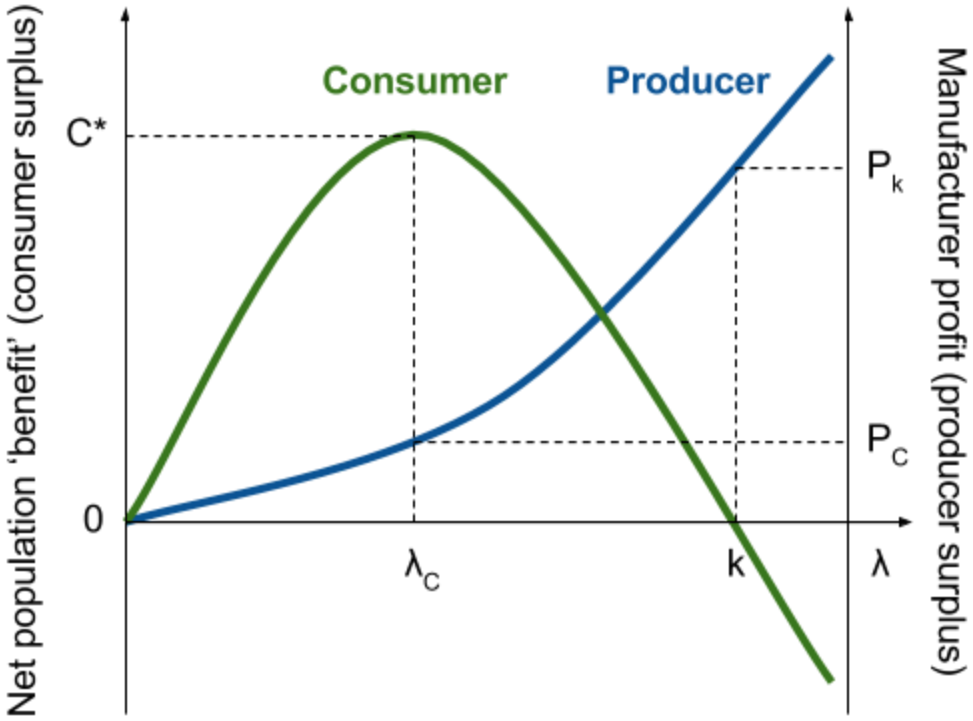


**Figure 3: Consumer and producer threshold curves, reflecting the relationship between the threshold (λ), net population 'benefit' (consumer surplus) and manufacturer profit (producer surplus)**

The relationship between changes in the threshold and the sign and direction of change for consumer surplus, producer surplus, and the *combined surplus* are summarized in **Table 1**.

Below a threshold of $\lambda_C$, consumer and producer surplus are both positive and both increase with the threshold; it follows that the combined surplus is also positive and increasing, regardless of the conversion rate used. An implication of this is that there is no reason to specify a threshold below $\lambda_C$, since a higher threshold would benefit both consumers and producers. (This implication is very similar to that from the Laffer curve, where the area to right of the peak is considered 'off-limits' since an identical tax revenue may be collected with a lower tax rate; here, the area to the left of the peak of the CTC may be considered 'off-limits' since consumer and producer surplus can both be increased by specifying a higher threshold).

Above a threshold of $\lambda_C$, but below a threshold of $k$, consumer surplus decreases but remains positive, while producer surplus increases still further. It follows that the combined surplus is also positive across this range, although its direction of change is ambiguous since this depends upon the *conversion rate* between consumer and producer surplus.

Above a threshold of $k$, consumer surplus becomes negative and continues decreasing thereafter, while producer surplus continues increasing. It follows that both the sign and the direction of change of the combined surplus are ambiguous across this range, since both now depend upon the conversion rate between consumer and producer surplus.

| Threshold range | Property | Consumer surplus | Producer surplus | Combined surplus |
|---|---|---|---|---|
| $0 < \lambda < \lambda_C$ | Sign | Positive | Positive | Positive |
| | Direction of change | Increasing | Increasing | Increasing |
| $\lambda_C < \lambda < k$ | Sign | Positive | Positive | Positive |
| | Direction of change | Decreasing | Increasing | Ambiguous |
| $\lambda > k$ | Sign | Negative | Positive | Ambiguous |
| | Direction of change | Decreasing | Increasing | Ambiguous |

**Table 1: Sign and direction of change for consumer surplus, producer surplus and combined surplus across different threshold ranges**

# Specification of ‘optimal’ thresholds

Given the inherent tension between consumer and producer interests, the specification of an ‘optimal’ threshold is a difficult task. It depends crucially upon the policy objective adopted, specifically the desired distribution of the combined surplus between consumers and producers.

The determination of this objective is a matter for policy makers, and so no specific objective will be assumed here. Nevertheless, it is useful to explore the implications of alternative objectives for the specification of the optimal threshold. We will therefore consider seven possible policy objectives and the optimal thresholds associated with each. In cases where we are unable to precisely determine the optimal threshold, we will instead specify a range in which the optimal threshold must lie, given the properties of each threshold curve described earlier.

## Policy objectives

A number of possible policy objectives exist, including (but not limited to) the following:

1. Maximize *consumer* surplus;
2. Maximize *consumer* surplus, subject to consumer and producer surplus each being *non-negative*;
3. Maximize *consumer* surplus, subject to *producer* surplus comprising a *guaranteed proportion of the combined surplus* and also subject to each being *non-negative*;
4. Maximize *producer* surplus;
5. Maximize *producer* surplus, subject to consumer and producer surplus each being *non-negative*;
6. Maximize *producer* surplus, subject to *consumer* surplus comprising a *guaranteed proportion of the combined surplus* and also subject to each being *non-negative*;
7. Maximize the *combined* surplus (consumer and producer surplus);
8. Maximize the *combined* surplus, subject to each being *non-negative*.

Satisfying objectives 1, 4 or 7 may require consumer or producer surplus to be *negative*, an outcome that might not be considered reasonable by patients or manufacturers. For example, it might be considered unreasonable to expect the health care system to adopt technologies that diminish net population ‘benefit’ in order to increase manufacturer profit, or to expect manufacturers to supply new technologies at a loss in order to provide ‘benefit’ to patients.

Objectives 2, 3, 5, 6 and 8 address these concerns by requiring that both consumer and producer surplus be non-negative. Objectives 3 and 6 also incorporate a concern for the *proportion* of the combined surplus that is allocated to consumers or producers. Note that the maximum surplus achievable may be less in the presence of each of these constraints.

| Policy objective | Optimal threshold, or range containing optimal threshold | Comments |
|---|---|---|
| 'Maximize *consumer* surplus' | $\lambda^* = \lambda_C$ | Consumer surplus is maximized by specifying a threshold of $\lambda_C$. |
| 'Maximize *consumer* surplus, subject to consumer and producer surplus each being *non-negative*' | $\lambda^* = \lambda_C$ | At a threshold of $\lambda_C$, consumer surplus is maximized and producer surplus is positive. |
| 'Maximize *consumer* surplus, subject to *producer* surplus comprising a *guaranteed proportion of the combined surplus* and also subject to each being *non-negative*' | $\lambda_C \leq \lambda^* \leq k$ | The proportion of the combined surplus allocated to producers increases above $\lambda_C$. If producer surplus comprises the required proportion of the combined surplus at $\lambda_C$ then this is the optimal threshold. If not, the threshold should be progressively increased until the required proportion is achieved |
| 'Maximize *producer* surplus' | $\lambda^* = \infty$ | Producer surplus is maximized with an infinitely high threshold. |
| 'Maximize *producer* surplus, subject to consumer and producer surplus each being *non-negative*' | $\lambda^* = k$ | Since producer surplus increases with the threshold, and consumer surplus is negative at any threshold above $k$, this objective is satisfied by specifying a threshold of $k$. |
| 'Maximize *producer* surplus, subject to *consumer* surplus comprising a *guaranteed proportion of the combined surplus* and also subject to each being *non-negative*' | $0 < \lambda^* \leq k$<br><br>OR<br><br>*N/A* | As above, except that the optimal threshold is derived by progressively lowering the threshold from $k$ until the required proportion of consumer surplus is achieved. If the threshold is lowered to zero and this proportion is still not achieved then no threshold exists that satisfies this objective. |
| 'Maximize the *combined* surplus (consumer and producer surplus)' | $\lambda^* > \lambda_C$ | Consumer and producer surplus both increase with the threshold up to $\lambda_C$. Above $\lambda_C$, consumer surplus falls and producer surplus increases. The optimal threshold therefore depends upon the shape of each threshold curve but must exceed $\lambda_C$. |
| 'Maximize the *combined* surplus, subject to each being *non-negative*' | $\lambda_C < \lambda^* \leq k$ | Since consumer and producer surplus both increase with the threshold up to $\lambda_C$, but consumer surplus is negative above $k$, the optimal threshold must lie between $\lambda_C$ and $k$. |

**Table 2: Optimal threshold (λ*), or range containing optimal threshold, for each objective**

## ‘Optimal’ thresholds for each objective

**Table 2** reports the optimal threshold ($\lambda^*$), or the range containing the optimal threshold, for each of the eight policy objectives considered above.

Where the objective is to maximize *consumer* surplus, the optimal threshold is $\lambda_C$. This finding holds if there is also a desire for producer surplus to be non-negative, since producer surplus is positive at this threshold. If, in addition, there is a desire that producer surplus comprise a guaranteed proportion of the combined surplus, this may require that the optimal threshold be increased above $\lambda_C$ (but no higher than $k$) until this proportion is reached.

Where the objective is to maximize *producer* surplus, the optimal threshold is infinitely high. However, this results in negative consumer surplus; if there is also a desire for consumer surplus to be non-negative, then the optimal threshold is $k$. If, in addition, there is a desire that consumer surplus comprise a guaranteed proportion of the combined surplus, this may require that the optimal threshold be lowered below $k$ until this proportion is reached.

Finally, where the objective is to maximize the *combined* surplus, the optimal threshold lies somewhere above $\lambda_C$, with its *precise* location dependent upon the shape of each threshold curve and the conversion rate between consumer and producer surplus. If there is also a desire that both consumer and producer surplus be non-negative, the optimal threshold lies somewhere above $\lambda_C$ but no higher than $k$.

# Discussion

This paper has proposed a new conceptual model of the cost-effectiveness threshold that accounts for strategic behaviour on the part of manufacturers and allows for consideration of 'optimal' thresholds under various policy objectives regarding the distribution of consumer and producer surplus. This proposal combines elements of conventional supply-side and demand-side approaches into a single model: the conventional supply-side threshold ($k$) forms one of two anchors of the consumer threshold curve, while the conventional demand-side threshold is used to convert consumer and producer surplus into a common metric.

Despite building upon these familiar foundations, the integration of strategic pricing behaviour into the model has resulted in implications that depart from those of conventional supply-side and demand-side approaches. The conventional supply-side approach has been shown to be consistent with only one of the eight policy objectives considered here: that of maximizing *producer* surplus subject to the constraint that consumer surplus is non-negative. This objective differs substantially from that which the supply-side approach is widely assumed to satisfy: maximizing net population 'benefit' (i.e., *consumer* surplus). It is debatable whether proponents of a conventional supply-side approach to the threshold would be in favour of adopting such an objective over some of the other objectives considered here; if an alternative policy objective is adopted, $k$ is not generally the optimal threshold to specify.

If the policy objective is to maximize *consumer* surplus, then a *lower* threshold than $k$ should be used: we define this as the 'optimal consumer threshold', $\lambda_C$. Specifying $\lambda_C$ requires an understanding of the shape of the consumer threshold curve; this in turn requires an empirical estimate of $k$ and also an understanding of the distribution of reserve ICERs across all new technologies. Although a number of recent studies have published empirical estimates of $k$, the latter consideration has not been subject to any empirical research to date. There is, therefore, a need for broadened empirical research if maximizing consumer surplus is the policy objective.

If policy is instead focussed upon maximizing *producer* surplus, then there is no limit as to how high the threshold should be set. Alternatively, if the focus is on maximizing producer surplus subject to a constraint that consumer surplus be non-negative, then the optimal threshold is $k$, since this is the highest threshold at which consumer surplus is non-negative.

## Limitations

The model proposed here is conceptual and makes a number of strong assumptions. It is expected that some of these assumptions may be explored and relaxed in future research. In particular, we have assumed that manufacturers are *perfectly* strategic, always increasing prices up to the threshold and never behaving in a way that does not maximize profits. This might not be entirely accurate.

Possible future advancements to the model include relaxing the assumption that the policy maker sets only a single threshold, allowing for future changes in the price of technologies (as drugs lose patent protection and generic competitors enter the market), and more complex reimbursement mechanisms (such as risk sharing schemes) that may also be subject to strategic behaviour on the part of manufacturers.

## Policy implications

The proposed model suggests that the optimal threshold is conditional upon a number of factors, including the policy objective, the conversion rate between consumer and producer surplus (a demand-side consideration), the shadow price of the health care budget constraint (a supply-side consideration), the distribution of reserve ICERs, and other factors that may affect the consumer and producer threshold curves.

Based on recent empirical estimates of supply-side thresholds (£12,936, €24,870 and AU$28,033 per QALY in England, Spain and Australia, respectively), the proposed model implies that, if decision makers in these countries have a primary concern for maximizing consumer surplus, then thresholds *lower* than these should be specified in practice. The use of *higher* thresholds is consistent with an objective of maximizing *producer* surplus, subject to a weak concern for consumer surplus that serves only to limit the extent to which it is negative.

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# Appendix

## Considering losses for non-supplying manufacturers

If the agency that specifies the cost-effectiveness threshold wishes to consider, within the calculation of producer surplus, the losses incurred by manufacturers that do *not* supply new technologies to the health care system, then this will have implications for the specification of the 'optimal' threshold under each policy objective. The purpose of this Appendix is to explore how the 'optimal' threshold might change when these losses are taken into consideration.

### The producer threshold curve

When these losses are taken into consideration, the producer threshold curve (PTC) is no longer entirely above the horizontal axis. This is because, at very low thresholds, these losses exceed the small profits enjoyed by manufacturers who supply new technologies to the health care system; it follows that the PTC is negative at very low thresholds.

As the threshold increases, profits for manufacturers who supply new technologies to the health care system increase, and eventually exceed the losses incurred by other manufacturers. At this point, the PTC intersects the horizontal axis and the producer surplus becomes positive. We will refer to the threshold corresponding to this point as the 'minimum producer threshold' ($\lambda_P$), since this is the minimum threshold at which producer surplus is non-negative.

The implication of considering these losses for the 'optimal' threshold depends upon *where* the PTC intersects the horizontal axis, and hence the value of $\lambda_P$ relative to $\lambda_C$ and $k$. There are three possible scenarios:

1. The PTC intersects the horizontal axis to the *left* of the peak of the CTC; it follows that the minimum producer threshold is less than the optimal consumer threshold, which in turn is less than $k$ ($\lambda_P < \lambda_C < k$). This implies that these losses are relatively *small*.
2. The PTC intersects the horizontal axis to the *right* of the peak of the CTC, but to the *left* of where the CTC intersects the horizontal axis; it follows that the minimum producer threshold exceeds the optimal consumer threshold but is still less than $k$ ($\lambda_C < \lambda_P < k$). This implies that these losses are *moderate*.
3. The PTC intersects the horizontal axis to the *right* of where the consumer's 'threshold curve' intersects the horizontal axis; it follows that the minimum producer threshold is higher than $k$, which in turn exceeds the optimal consumer threshold ($\lambda_C < k < \lambda_P$). This implies that these losses are relatively *large*.

The 'optimal' thresholds under each scenario, for each policy objective, are summarized in

**Table 3**. The modified PTCs are plotted in **Figure 4**, **Figure 5** and **Figure 6**, respectively.

| **Policy objective** | **Optimal threshold, or range containing optimal threshold** | | |
|---|---|---|---|
| | **Scenario 1** | **Scenario 2** | **Scenario 3** |
| 'Maximize *consumer* surplus' | $\lambda^* = \lambda_C$ | $\lambda^* = \lambda_C$ | $\lambda^* = \lambda_C$ |
| 'Maximize *consumer* surplus, subject to consumer and producer surplus each being *non-negative*' | $\lambda^* = \lambda_C$ | $\lambda^* = \lambda_P$ | *N/A* |
| 'Maximize *consumer* surplus, subject to *producer* surplus comprising a *guaranteed proportion of the combined surplus* and also subject to each being *non-negative*' | $\lambda_C \le \lambda^* \le k$ | $\lambda_P \le \lambda^* \le k$ | *N/A* |
| 'Maximize *producer* surplus' | $\lambda^* = \infty$ | $\lambda^* = \infty$ | $\lambda^* = \infty$ |
| 'Maximize *producer* surplus, subject to consumer and producer surplus each being *non-negative*' | $\lambda^* = k$ | $\lambda^* = k$ | *N/A* |
| 'Maximize *producer* surplus, subject to *consumer* surplus comprising a *guaranteed proportion of the combined surplus* and also subject to each being *non-negative*' | $\lambda_P < \lambda^* \le k$ | $\lambda_P < \lambda^* \le k$ | *N/A* |
| 'Maximize the *combined* surplus (consumer and producer surplus)' | $\lambda^* > \lambda_C$ | $\lambda^* > \lambda_C$ | $\lambda^* > \lambda_C$ |
| 'Maximize the *combined* surplus, subject to each being *non-negative*' | $\lambda_C < \lambda^* \le k$ | $\lambda_P < \lambda^* \le k$ | *N/A* |

**Table 3: Optimal threshold (λ*), or range containing optimal threshold, for each objective when losses for non-supplying manufacturers are considered**

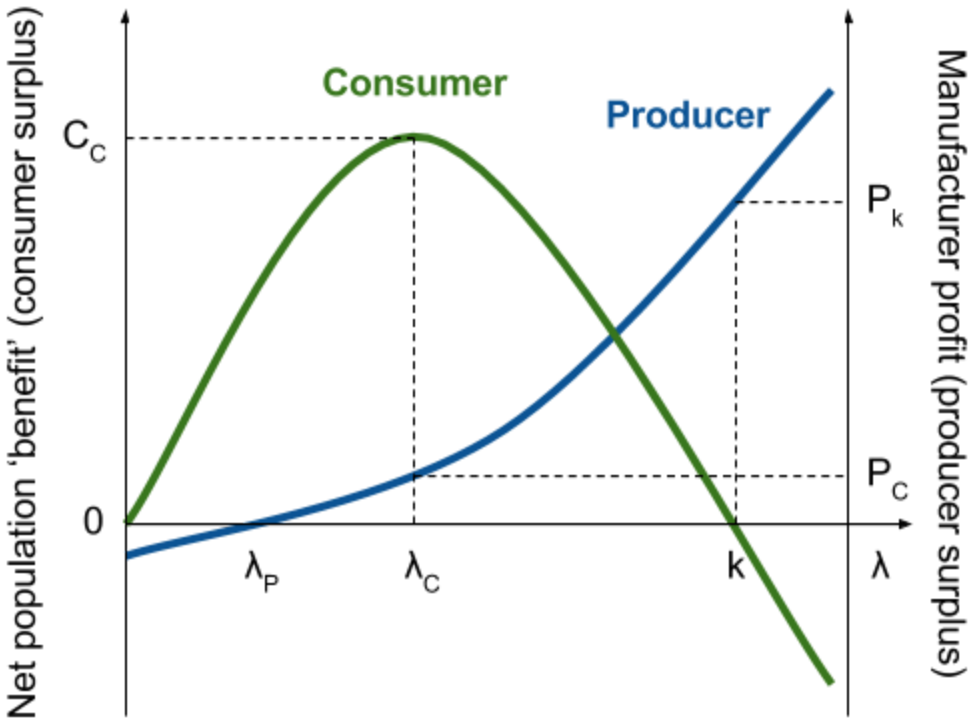



**Figure 4: Consumer and producer threshold curves when losses for non-supplying manufacturers are considered and these losses are small ($\lambda_P < \lambda_C < k$) (Scenario 1)**

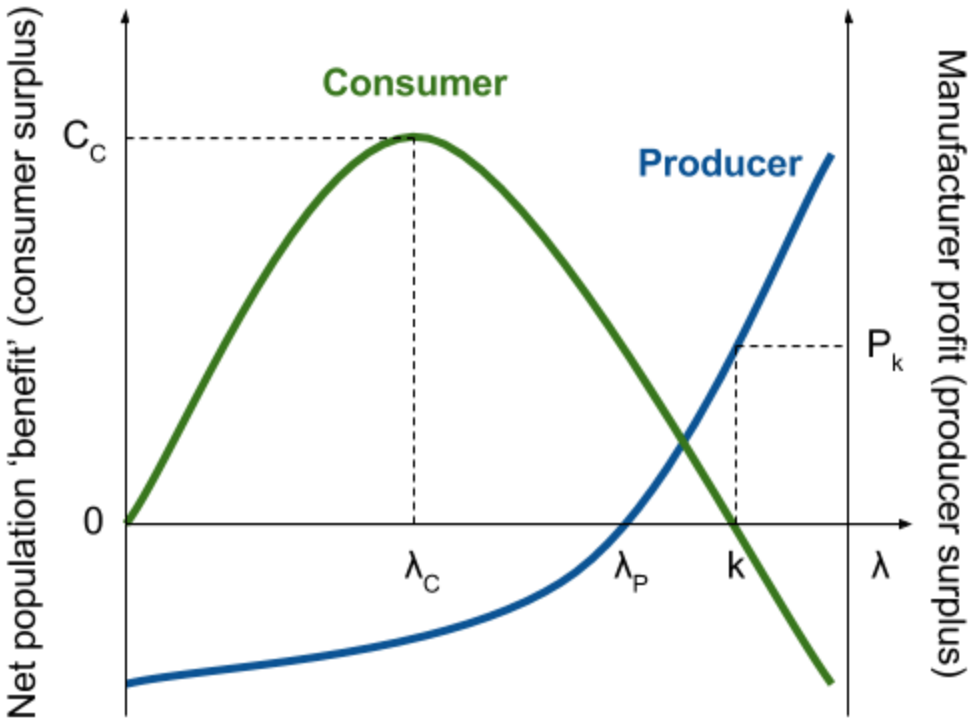



**Figure 5: Consumer and producer threshold curves when losses for non-supplying manufacturers are considered and these losses are moderate ($\lambda_C < \lambda_P < k$) (Scenario 2)**

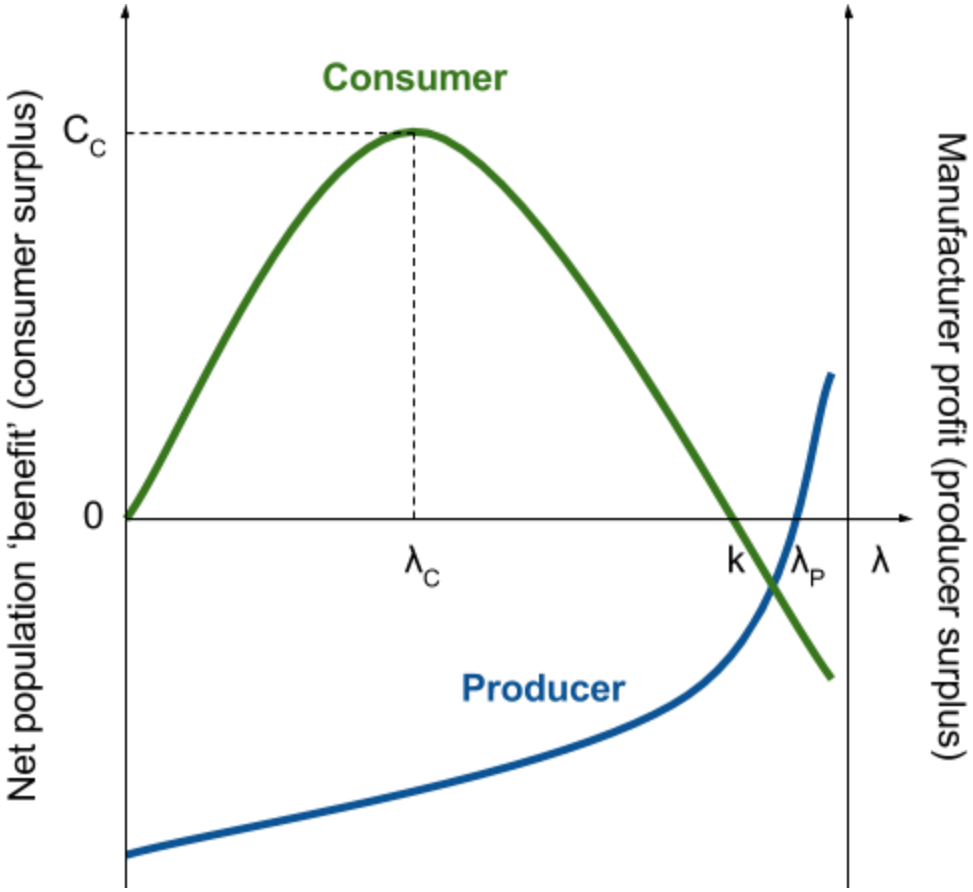



**Figure 6: Consumer and producer threshold curves when losses for non-supplying manufacturers are considered and these losses are large ($\lambda_C < k < \lambda_P$) (Scenario 3)**

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# PMPRB GUIDELINES SCOPING PAPER

## High Level Overview of Potential New Framework

**CGI CONSULTATION PHASE**

Canada

# CONTENTS

# INTRODUCTION

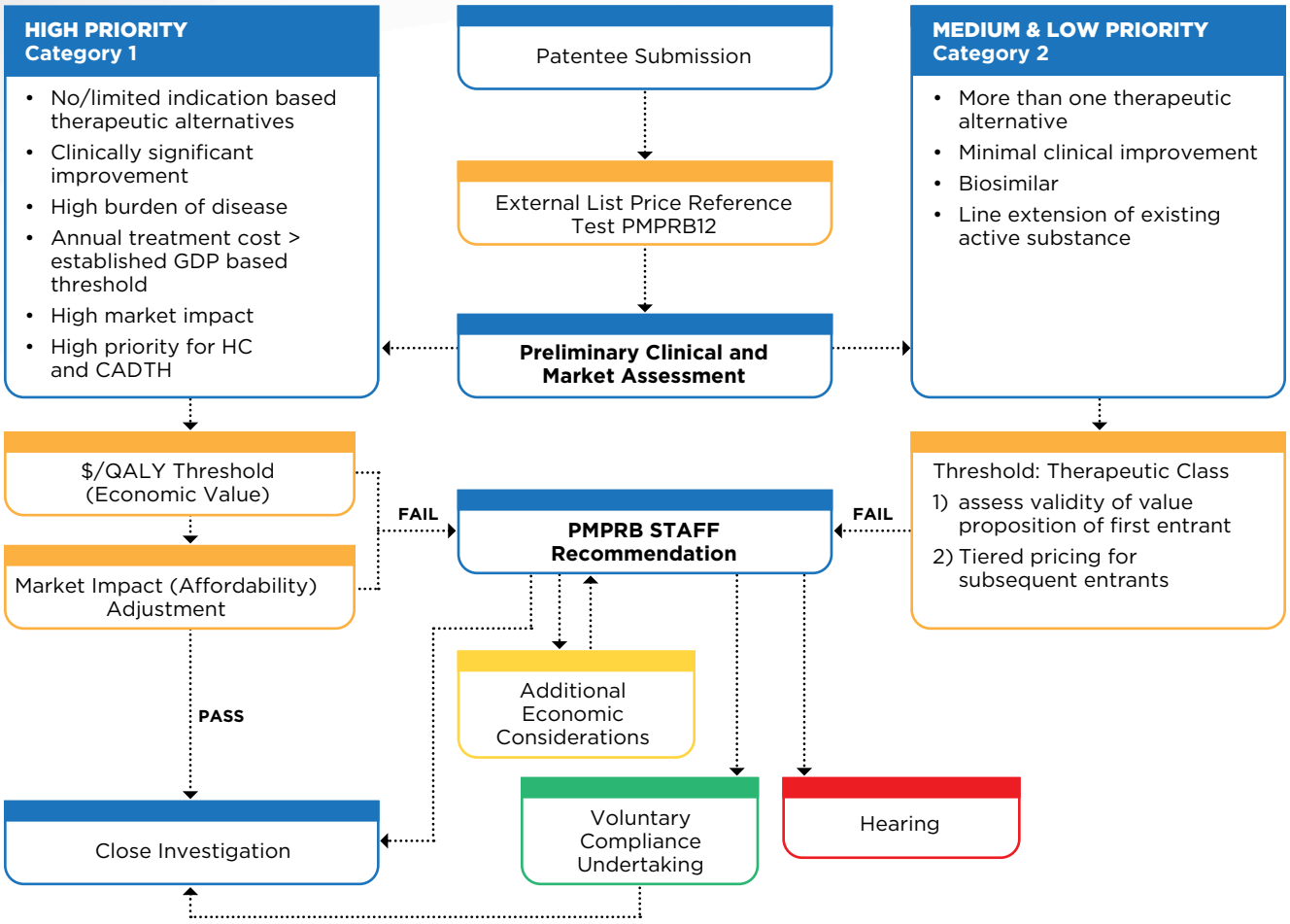
This scoping paper is intended to be read in conjunction with proposed amendments to the *Patented Medicines Regulations* ("Regulations"), and accompanying Regulatory Impact Analysis Statement (RIAS), which were pre-published in the December 2nd, 2017 issue of the Canada Gazette, Part I. Its purpose is to provide stakeholders and interested members of the public with an outline of the PMPRB's preliminary thoughts on how best to operationalize the proposed changes to the Regulations, through non-binding Guidelines as contemplated by s.96 of the *Patent Act*, within the context of the existing and proposed legislation and the PMPRB's ongoing efforts at reform. It is hoped that this document will serve as a catalyst for a more informed, focussed and productive consultation process on framework modernization, with a view to having new Guidelines in place by early 2019. This document is not to be viewed as a definitive interpretation of the current or proposed legislation or of the RIAS for the proposed amendments by the PMPRB, is not the Government's expression of policy intent or an official part of the Canada Gazette I (CGI) consultation, and is not intended to bind the PMPRB or the Government in the application and interpretation of legislation. The PMPRB will officially consult on a revised set of proposed Guidelines in the spring of 2018.

# THE NEW FRAMEWORK

As an expert economic regulatory body, the PMPRB must ensure that its new framework is grounded in sound and prevailing economic theory. In conceiving the mechanics of that framework, the PMPRB was mindful of the Minister of Health's stated policy rationale for the proposed regulatory amendments and of the overarching purpose of the current and proposed legislation. The PMPRB also sought to give effect to areas of stakeholder agreement that emerged from the recent Guidelines modernization consultation. Accordingly, to the extent possible, the framework envisaged by the PMPRB employs economically-derived, bright line tests to yield meaningful ceiling prices that are foreseeable to patentees. As before, the new Guidelines are proffered as rules of general application which serve as a mechanism for determining a rough estimate of where the line between potential non-excessive prices and potential excessive prices should be drawn by PMPRB staff. The objective of the Guidelines is to enable the calculation of a national ceiling price above which it would be unreasonable for any consumer in Canada to pay, not an ideal price for each payer based on their individual ability and willingness to pay.

While the details of the framework remain to be worked out through consultation, its basic structure can be described as a risk-based approach to pricing review that is broken down into five main parts, as illustrated in the following schematic and discussed in more detail below.

## PROPOSED PRICE REVIEW SCHEMATIC*




*For discussion purposes only, not intended to bind or limit the PMPRB or the Government in the application and interpretation of legislation

## Part I: Interim international price reference test

At introduction, all new drugs would first be subject to an interim price test based on the list price of a new drug in Canada against the list price in the proposed PMPRB12 basket of countries. Domestic and international list prices in today's environment of confidential discounts and rebates represent the starting point of a price negotiation rather than a true reflection of actual price paid in the market place. In this context, the PMPRB would look at how the proposed price in Canada compares to public list prices in other markets. If the price in Canada exceeds the median of the PMPRB12, it would be considered potentially excessive.

## Part II: Screening

The second part of the framework consists of a screening phase which would classify new patented drugs as either high or low priority based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans). At this stage in the process, the PMPRB would consider whether the drug is first in class, has few or no therapeutic alternatives, provides significant therapeutic improvement over existing treatment options, is indicated for a condition that has a high prevalence in Canada, is a high cost drug (i.e. an average annual cost higher than a GDP-based threshold) or is classified as a high priority drug by other agencies/regulators in the health care system (such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or Health Canada) because of unmet medical need. Drugs that appear to be high priority based on these screening factors would be subject to automatic investigation and a comprehensive review to determine whether their price is potentially excessive.

## Part III: High priority drugs

Once a drug is assessed as high priority, the third part of the new framework would see the PMPRB apply a two-part test for evaluating potential excessivity[1].

The first part of the test would assess the incremental cost per quality-adjusted life year (QALY) of the drug, as determined by CADTH's health technology assessment process, against an explicit cost effectiveness threshold. The threshold would be based on the opportunity cost associated with displacing the least cost effective health technology in the Canadian health system, otherwise understood as the marginal cost of a QALY, as calculated by expert health economists and revised periodically to reflect changing market conditions. Drugs that prolong life or provide significant QALY gains could be subject to a more generous threshold, as Canadian payers have demonstrated a higher willingness to pay for these types of drugs.

The second part of the test would assess whether a drug that meets the cost effectiveness threshold should have its price further adjusted because of its expected impact on payers within the first three to five years from launch (assuming appropriate clinical utilization and no rationing of care). This test would consider the anticipated market size of the new drug against GDP growth, with the latter serving as a rough proxy for how much Canadian consumers can afford to pay for the new patented drugs that come to market on an annual basis. The test could also be used to allow a price adjustment upward in instances where a drug has a very high opportunity cost but very small market impact due to the extreme rarity of the condition it is indicated to treat.

[1] The test addresses current factors that the PMPRB must consider under s.85 of the *Patent Act* as well as the new factors that are identified in the proposed amendments to the Regulations published on December 2, 2017.

If the price fails this two-part test, the patentee would be provided with an opportunity to explain why the price of its drug is not excessive having regard to the cost of making or marketing it or such other economic factors it believes are relevant in the circumstances. Patentees would be permitted to provide confidential commercial information in support of their position, including true prices in the PMPRB12 and proposed non-transparent rebates and discounts to direct and indirect payers in Canada. If the outcome of the above process is a determination that the price of the drug is potentially excessive:

- Its public ceiling price would continue to be set by international price referencing; but
- the ceiling price resulting from the application of the two-part test would be kept confidential.

Patentees will be required to report price and revenue information to the PMPRB net of direct or indirect third party discounts or rebates. This will ensure that the PMPRB is fully informed of the actual prices for patented drugs in Canada but also enable patentees to comply with much lower ceiling prices under the new framework.

## Part IV: Medium and low priority drugs

The fourth part of the new framework would apply to medium and low priority drugs. Drugs in this category would be expected to have a minimum number of therapeutic alternatives and offer little or no therapeutic improvement over the standard of care. Drugs considered to be medium priority would be subject to the same initial price test as high priority drugs, such that they would be considered potentially excessive if their public list price is above the median of public list prices in the PMPRB12 countries. For this class of drugs, the PMPRB could employ a revised therapeutic class comparison test that requires each successive entrant to reduce its price relative to the price of the drug that preceded it. Again, patentees would be provided with the opportunity to explain why a higher price is justified based on the same economic factors that are considered relevant for high priority drugs.

Drugs categorized as low priority, because of the presence of a significant number of therapeutic alternatives in the market and/or generic competition, would not be subject to an introductory or ongoing s.85 analysis and would be investigated on a complaints basis only.

## Part V: Re-benching

The fifth and final part of the new framework would involve the periodic "re-benching" of drugs to ensure that previous determinations of potential excessive pricing and/or price ceilings remain relevant in light of new indications (resulting in a change of market size) or changes in market conditions. Depending on the nature of the change, the re-benching process could result in a decrease or increase in ceiling price.

# CONCLUSION

If passed in their current form, the proposed amendments would allow the PMPRB to move to a risk-based framework that scrutinizes drugs with the greatest potential for excessive pricing and takes into account both their value to, and financial impact on, consumers in the health system when setting ceiling prices. This would constitute a paradigm shift in how the PMPRB regulates patented drug prices but would not depart from or expand on its original mandate.

By explicitly requiring the PMPRB to consider the new proposed factors, policy makers have recognized that price alone does not provide sufficient context by which to evaluate excessive pricing in the current climate. Specifically, price divorced from value, cost and affordability does not capture key inputs in determining what the impact of a drug will be on payers or on total population health. These are critical considerations in an era marked by increasingly constrained health budget envelopes, an aging population and an ever increasing number of drugs with annual average treatment costs in the hundreds of thousands of dollars.

It should be emphasized that the above described framework is only notional at this stage and may change as a result of any differences between the proposed amendments and the final Regulations or in response to stakeholder feedback from PMPRB-led consultations on Guideline reform.


# NEXT STEPS

In the coming weeks, Health Canada and the PMPRB will be hosting multi-stakeholder webinars where the department will address the proposed regulatory amendments and the PMPRB will address the changes discussed in this scoping paper. The PMPRB will also be making Guideline reform the focus of its upcoming annual outreach sessions for patentees to be held in January of 2018. It is expected that a first draft of the PMPRB's new Guidelines will be made public in the spring of 2018, with technical roundtables to be scheduled shortly thereafter. However, at this stage of the process, the PMPRB is specifically encouraging stakeholders to reflect on the following questions in order to prepare for upcoming consultations on a revised set of proposed Guidelines:

1. What considerations should PMPRB use in screening drugs for high priority?
2. To what extent should low priority drugs be scrutinized?
3. How should a cost effectiveness threshold be established?
4. Should the application of a threshold be subject to further adjustment depending on market size considerations?
5. How should re-benching work and when should it occur (and to what drugs)?
6. What price tests should the PMPRB apply to the new PMPRB12?
7. How should the PMPRB make use of confidential third party pricing information?

# FURTHER INFORMATION

Questions or clarifications on the content of this document can be submitted by email, letter mail or fax to:

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Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# Second Meeting Steering Committee

## August 15, 2018

Canada

# Agenda

- Summary of Working Group Meeting
- Review written feedback
- Topics for Discussion
  - Use of External Price Referencing
  - Use of List and Net Price Ceilings
  - Risk Assessment and Prioritization Criteria for Category 1 & 2 medicines
  - Re-Benching Criteria
- Review need for additional WG

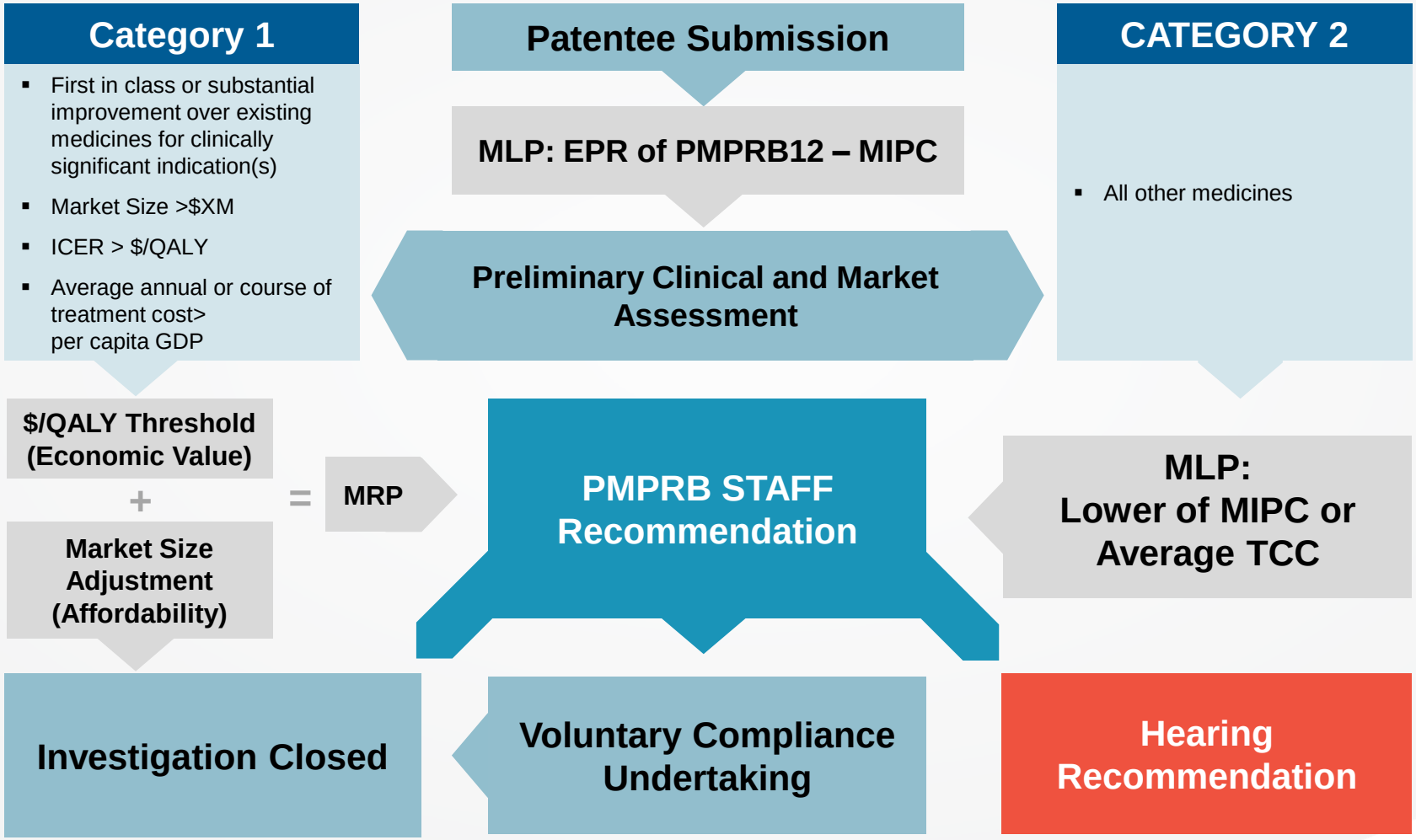
# Summary of Technical Working Group (TWG) Meeting and Next Steps

- The first meeting of the TWG was held July 26, 2018 in Ottawa.
- The Terms of Reference were agreed upon by all members present.
- Board Staff presented the proposed PMPRB framework modernization structure to the members.
- Members discussed each of the topics designed to elicit specific economic feedback.
- It was agreed that subsequent meetings will be scheduled to discuss each topic in further detail. Members were surveyed for availability in advance of selecting dates for the next meeting.

# Written Feedback Received to Date

- IMC, BIOTECanada, and CORD have provided written submissions on the nature and scope of the Steering Committee's work.
- At a high level, these submissions have requested a roadmap for SC meetings, a need for case study discussion, and a number of operational questions related to the proposed framework.
- Additional working groups on specific topics have also been recommended by BIOTECanada.
- The roadmap for future meetings presented to the SC on July 24 is intended to reflect this feedback. Specific operational questions will be raised and addressed in the course of topic and case study discussion.
- The need for additional working groups will also be reviewed as part of the SC's discussion of these topics.

# Proposed PRICE Review Schematic



# Use of External Price Referencing
# Part 1: Median international price test (MIPC)

- The proposed approach is that all new medicines are assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).

- The MIPC would be recalculated annually until there are at least 7 countries or 3 years post first date of sale. At that point the MLP would no longer be interim. This approach provides both predictability (e.g., exchange rate fluctuations) and reduces regulatory burden.

- Re-benching could result in the MLP being adjusted over time.

- IMS will be used to verify international list prices however filing requirements for patentees will remain unchanged for the new schedule.

# Use of External Price Referencing Question for Consideration

- Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?
- Should exceptions be made to the MLP-MIPC test and, if so, when and why?
- Should there be a price floor for Category 2 medicines based on LIPC?
- Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?
- Should an increasing gap between MIPC and the MLP trigger a re-bench?
- Should EPR differ depending on category or vintage of the patented medicine?
- Additional questions from SC?

# Use of List and Net Price Ceilings

- The conceptual framework presented to the SC at the first meeting proposed the establishment of two ceilings for Category 1 medicines based on both list (MLP) and net (rebated) prices (MRP).

- For Category 2 medicines, the proposal is to establish one ceiling (MLP) based on list prices domestically and internationally based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC). No Category 2 medicine will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).

- The approach aims to establish a net price ceiling to both protect Canada's true transaction price from being exposed and allow patentees to comply with the net price ceilings through use of all discounts/rebates direct and indirect.

# Use of List and Net Price Ceilings

- Should a Category 1 medicine ever have more than one MRP?
- Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?
- Should confidential third party pricing information only be used for compliance purposes?
- Additional questions from SC?

# Risk Assessment and Prioritization Criteria for Category 1 & 2 Medicines

- The second part of the framework consists of a screening phase which would classify new patented medicines as either high or low priority based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans).
- The framework proposed high level criteria that PMPRB would use to categorize medicines as Category 1 or 2:
  - First in class or substantial improvement over existing medicines for clinically significant indication(s)
  - Market Size >Affordability Threshold
  - ICER > maximum opportunity cost threshold
  - Annual or treatment cost> per capita GDP
- medicines that appear to be high priority based on these screening factors would be subject to automatic investigation and a comprehensive review to determine whether their price is potentially excessive.

# Risk Assessment and Prioritization Criteria for Category 1 & 2 Medicines

- Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?
- Should further categories exist with different treatment modalities?
- Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?
- Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?
- Should Category 2 medicines be scrutinized more or less than proposed?
- Other questions proposed by SC?

# Re-Benching Criteria

- All new medicines will be given an interim MLP of 3 years or until the medicine is sold in 7 countries, whichever comes first.
- MLP is then frozen, as is MRP, unless re-benching is triggered by one of the following criteria:
  - Approval of a new indication
  - Sales in excess of expected market size
  - New evidence on cost-effectiveness (e.g. CADTH therapeutic class review or lifting of HC conditions on NOC)
  - Significant changes in international prices (eg. MIPC < MIPC at intro by more than 25%)
- Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI

# Re-Benching Criteria

- Complaints received by the PMPRB will trigger an investigation, during which the PMPRB will assess whether:

  - The medicine is in compliance with the Guidelines; and
  - whether circumstances in the market have changed to warrant a rebenching/reclassification.

# Re-Benching Criteria

- How often and in what circumstances should a medicine be rebenched?
- Other questions proposed by SC?

# Need for Additional Working Group

- Feedback to date suggest that the PMPRB consider establishing other working groups to deal with specific issues.

- Many of the issues flagged to date are administrative in nature and would likely be better situated for a working group in a later phase of the guidelines development process (similar to DIP Working Group).

- Are there specific high-level framework topics that the SC believes are not being addressed by the SC or the existing TWG?

# Next SC Meeting

- The next meeting will take place early September.

- PMPRB staff will respond to a summary of written feedback received from members following this meeting and lead a discussion on the following themes:

  - Tests for Category 1 medicines
  - Tests for Category 2 medicines
  - Use of confidential pricing information
  - Application of new regime to existing medicines

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# Data Analysis to Inform Guidelines Modernization SC and TWG

August 27, 2018

Canada

# Topic 1: Use of External Price Referencing

**Description provided in August webinar:**

- The MIPC would be recalculated annually until there are at least 7 countries or 3 years post first date of sale.  At that point the MLP would no longer be interim and patentees and consumers would have certainty as to the PMPRB MLP.

**Question posed:**

- Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?

# Topic 1: Use of External Price Referencing

**Data analysis:**

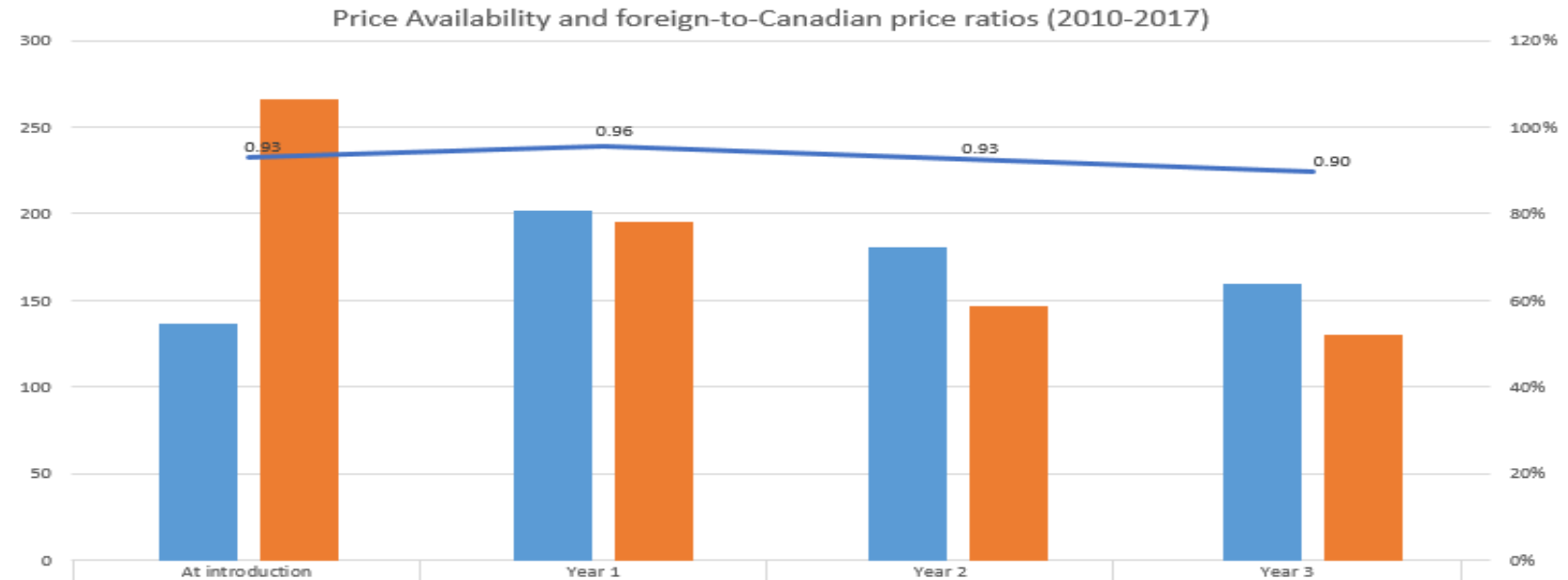
Using PMPRB data, a sample of patented medicines introduced between 2010 and 2017 were identified. MIDAS was used to identify prices in the new proposed PMPRB12 basket to assess:

- the distribution of medicines with less or more than 7 prices available within the first 3 years;
- the average foreign to Canadian price ratios; and
- the average number of countries that were available to calculate the MIPC.

**Findings:**

- More than 50% of patented medicines would have at least 7 prices and a final MLP based on the MIPC within first year of sales in Canada.
- These medicines accounted for almost 90% of total revenues.
- The average Foreign-to-Canadian price ratio was 0.90 after three years.

# External Price Reference (PMPRB12) Analysis




| | At introduction | Year 1 | Year 2 | Year 3 |
|---|---|---|---|---|
| Number of new products with at least seven foreign prices available | 137 | 202 | 181 | 160 |
| Number of new products with less than seven foreign prices available | 266 | 195 | 147 | 130 |
| Average foreign-to-Canadian price ratio- overall | 0.93 | 0.96 | 0.93 | 0.90 |
| Average foreign-to-Canadian price ratio- at least seven foreign prices available | 0.93 | 0.97 | 0.94 | 0.90 |
| Average number of countries included- at least seven foreign prices available | 9 | 9 | 10 | 10 |
| Average foreign-to-Canadian price ratio- less than seven foreign prices available | 1.04 | 0.90 | 0.79 | 0.83 |
| Average number of countries included- less than seven foreign prices available | 4 | 4 | 3 | 4 |
| Average share of Canadian revenues- at least seven foreign prices available | 70% | 88% | 85% | 83% |

PMPRB data

# Topic 3: Risk Assessment and Prioritization for Category 1 and Category 2 Medicines

## Description provided in August webinar:

- The framework proposed high level criteria that PMPRB would use to categorize drugs as Category 1 or 2:
  - First in class or substantial improvement over existing drugs for clinically significant indication(s)
  - Market Size > Affordability Threshold
  - ICER > maximum opportunity cost threshold
  - Annual treatment cost > per capita GDP

## Question posed:

- Is the proposed division and treatment of Category 1 and Category 2 drugs a reasonable risk-based regulatory approach?

# Impact of Various Scenarios for Screening Category 1 Medicines, 2010-2017

| Scenario | Market Size Threshold | Market Impact Years | ICER Threshold Screen (not applied) | Total % Patented Medicines Screened as Category 1 | % captured by Market Size Screen | % captured by Break-through/ Substantial improvement Screen | % captured by High cost drugs ($50K ~GDP/ Capita) Screen |
|---|---|---|---|---|---|---|---|
| 1 | 20M | Within any of the first 3 years | 0 | 22% | 16% | 7% | 4% |
| 2 | 40M | Within any of the first 3 years | 0 | 17% | 8% | 7% | 4% |
| 3 | 20M | Within any of the first 5 years | 0 | 27% | 21% | 7% | 4% |
| 4 | 40M | Within any of the first 5 years | 0 | 20% | 12% | 7% | 4% |

- Based on an analysis of PMPRB data (2010-2017), 309 patented medicines were analyzed using the proposed criteria other than the ICER threshold.
- $20M and $40M within any of the first 3 or 5 years was used to estimate impact of market size, capturing 8-21% of medicines.
- 7% of medicines would have been Category 1 based on being breakthrough or substantial improvements.
- 4% had a treatment cost above GDP/capita ($50K).
- The total percentage of medicines screened in would be 17% to 27%.
- Analysis is based on existing PMPRB pricing data (which excludes 3rd party discounts) and is thus likely an overestimate.

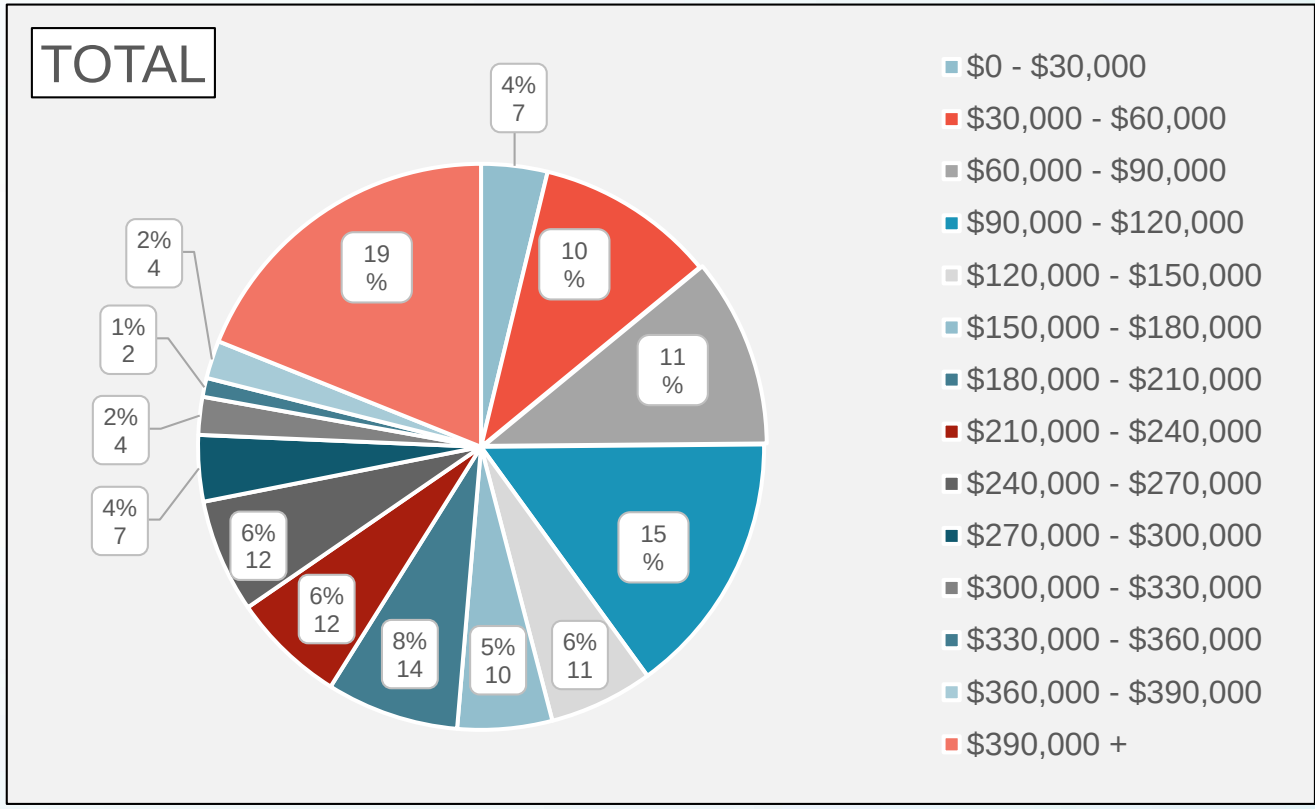
**Source:** PMPRB; HDAP reports; IQVIA Private Pay Direct Drug Plan Database, 2017

# Analysis of Canadian ICER Values

- Data presented is intended to inform the discussion of using ICER thresholds as both a screen and a price ceiling test for Category 1 medicines.
- Data compiled from publicly available CDR and pCODR reports published on CADTH's website dating back to 2008 and 2012 respectively.
- Includes CDR (n=102) and pCODR (n=83) data with available ICER values and a final recommendation date of July 2017 or prior.
- Recently published data on Canadian ICER values also provided for information.

# CADTH Total ICER Distribution

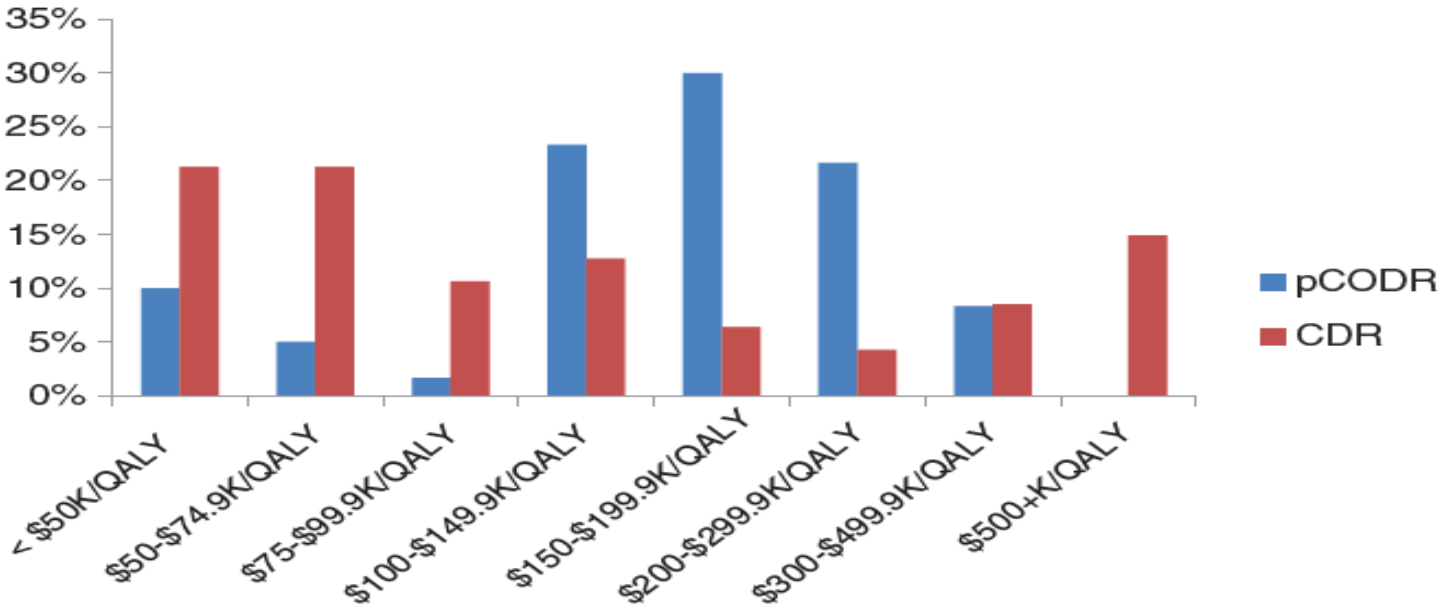
| Range ($/QALY) | pCODR (N) | pCODR (%) | CDR (N) | CDR (%) | Total (N) | Total (%) |
|---|---|---|---|---|---|---|
| $0 - $30,000 | 2 | 2% | 5 | 5% | 7 | 4% |
| $30,000 - $60,000 | 3 | 4% | 16 | 16% | 19 | 10% |
| $60,000 - $90,000 | 3 | 4% | 17 | 17% | 20 | 11% |
| $90,000 - $120,000 | 9 | 11% | 19 | 19% | 28 | 15% |
| $120,000 - $150,000 | 6 | 7% | 5 | 5% | 11 | 6% |
| $150,000 - $180,000 | 8 | 10% | 2 | 2% | 10 | 5% |
| $180,000 - $210,000 | 12 | 14% | 2 | 2% | 14 | 8% |
| $210,000 - $240,000 | 8 | 10% | 4 | 4% | 12 | 6% |
| $240,000 - $270,000 | 10 | 12% | 2 | 2% | 12 | 6% |
| $270,000 - $300,000 | 5 | 6% | 2 | 2% | 7 | 4% |
| $300,000 - $330,000 | 4 | 5% | 0 | 0% | 4 | 2% |
| $330,000 - $360,000 | 2 | 2% | 0 | 0% | 2 | 1% |
| $360,000 - $390,000 | 2 | 2% | 2 | 2% | 4 | 2% |
| $390,000 + | 9 | 11% | 26 | 25% | 35 | 19% |
| Total | 83 | 100% | 102 | 100% | 185 | 100% |



# Other sources of CADTH ICER values

- 206 drug-indication pairings from pCODR and CDR reports
- 75% of pCODR drugs fell between $100k-$300k/QALY
- 55% of CDR drugs were below $100k/QALY

**FIG. 2** Distribution of HTA-Recalculated ICERs by HTA Agency.




Source: A. Rocchi & F. Mills (2018), Activities of the pCPA: An observational analysis. Journal of Population Therapeutics & Clinical Pharmacology. Vol 25(2):e12-e22; August 7, 2018.

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# Third Meeting Steering Committee

## September 12, 2018

Canada

# Agenda

- Approval of agenda
- Approval of minutes from August 15th meeting
- Update on roadmap and discussion of PMPRB analysis
- Status of Technical Working Group deliberations
- Topics for discussion
  - Tests for Category 1 medicines
  - Tests for Category 2 medicines
  - Use of confidential pricing information
  - Application of new regime to existing medicines
- Next Meeting

# Update on Roadmap

- Written and oral feedback on all topics will be compiled in a final report.
- Draft report will be prepared for SC review after case study meeting.
- Feedback outside the scope of the proposed framework will be included in an annex as part of the public record.
- SC members will have an opportunity to provide feedback on all the topics until the report is finalized.
- Next meeting on case studies will be held in person in Ottawa.

# Discussion of PMPRB Analysis

- PMPRB provided additional data to SC members on August 27
- Analysis focused on:
  - Distribution of medicines with more or less than 7 PMPRB12 countries to set the MLP
  - Impact of potential market size, clinical, and cost screens to classify Category 1 medicines
  - Analysis of Canadian ICER values
- Do SC members have additional comments or questions on this data?

# Status of Technical Working Group (TWG)

- August 22-24th 7 teleconference calls, 6 topic-specific breakout sessions and one meeting of entire TWG.
  - Topic 1: Options for determining which medicines fall into Category 1
  - Topic 2: Application of supply-side cost effectiveness thresholds in setting ceiling prices for Cat 1 medicines
  - Topic 3: Establishing price ceiling for medicines with multiple indications
  - Topic 4: Accounting for uncertainty
  - Topic 5: Perspective
  - Topic 6: Options for price ceiling adjustment based on market size factor
- Further feedback has been/will be received in writing
- SC will see final TWG report in October; option for chair to present and Q&A

# Approach for Today's Meeting

- Refresher on the proposed framework
- Second set of discussion topics will be presented
- SC members can seek clarification of any points in advance of providing feedback
- Written feedback will be solicited on all topics

# Overview of new Guidelines framework

- A risk-based approach to price regulation that considers value and affordability, in addition to list prices in other like-minded countries.
- Basic structure can be broken down into 5 parts:
  - Part I: 'Maximum List Price' (MLP*) for all new medicines at introduction based on median of PMPRB12 (MIPC)
  - Part II: Screening of medicines into high priority (Category 1) or low priority (Category 2)
  - Part III: 'Maximum Rebated Price' (MRP**) for Category 1 medicines based on new pharmacoeconomic, market size and GDP factors
  - Part IV: Lower of MIPC and average of Therapeutic Class (ATCC) for Category 2 medicines
  - Part V: Re-benching

* *The MLP will be a ceiling based on public list prices.*

** *The MRP, which applies to Category 1 medicines only, would be applied to a medicine's average transaction price (ATP) net of all direct and indirect discounts and benefits.*

# Tests for Category 1 Medicines

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).
- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

# Step 1: Pharmacoeconomic Factor

- Empirical work undertaken by Karl Claxton at the University of York suggests a $30K/QALY opportunity cost threshold for Canada.

- Category 1 medicines would be assessed against a baseline threshold of $60K/QALY*.

- Medicines that meet certain clinical characteristics (e.g., high burden of disease or significant absolute gain in QALY) may warrant a higher threshold.

**To account for the variation in QALY values across the Provinces and Territories identified in the Claxton report and in keeping with the PMPRB's mandate as a ceiling price regulator.*

# Step 2: Market Size and GDP

- A Category 1 medicine may require a price adjustment beyond the $/QALY threshold if there are short term affordability concerns based on the medicine's expected use.
- Using the contribution of new medicines to GDP and GDP growth over the last five years, the PMPRB has estimated an initial market size threshold of $20M per new medicine.
- New Category 1 medicines with an estimated market size that is expected to exceed this threshold within any of their first five years of sale would have their MRP reduced by an additional percentage.
- The $20M threshold would increase based on GDP growth and/or CPI.

# Application of new factors to Category 1 Medicines

| Type of review | $/QALY target to set MRP | Market impact adjustment |
|---|---|---|
| **Baseline (market size up to $20M)** | $60K | N/A |
| **"Premium" (e.g. high burden, EDRD, significant absolute QALY gain)** | $90K to $150K | N/A |
| **High Impact (market size over $20M)** | $60K | 10% reduction on MRP for each additional $10M market size (to 50% maximum) |

# Questions: Tests for Category 1 Medicines

- Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?
- Should exceptions be made to the MIPC test and, if so, when and why?
- Should the cost effectiveness threshold for Category 1 drugs vary?
- Should a Category 1 medicine ever have more than one MRP?
- Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?

# Tests for Category 2 Medicines

- Category 2 medicines have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex-factory) prices, domestically and internationally.

# Questions: Tests for Category 2 Medicines

- Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?
- Should exceptions be made to the MIPC test and, if so, when and why?
- Should there be a price floor for Category 2 drugs and, if so, should it be based on LIPC?
- Should Category 2 drugs be scrutinized more or less than proposed?

# Use of Confidential Pricing Information

- Price reviews would be conducted for the following customer classes:
  - National/Provincial Retail – list price assessed against MLP
  - National Private Payer – ATP assessed against MRP
  - Provincial Public Payer – ATP assessed against MRP in each market
- ATPs are calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

# Questions: Use of Confidential Pricing Information

- Are the proposed definitions of markets and customer classes reasonable?
- Is the proposal to use third-party pricing information for compliance with the MRP reasonable?
- Other questions proposed by SC members?

# Application of New Regime to Existing Medicines

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 drugs would be re-benched later unless a complaint is received.
- All drugs within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to come into compliance.

# Questions: Application of New Regime to Existing Medicines

- Is the use of MIPC as an interim ceiling reasonable?
- Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?
- Are there reasonable alternative approaches to bringing existing medicines under the new framework?
- Other questions proposed by SC members?

# Additional Questions for Consideration

- Are there opportunities to further reduce regulatory burden while still operationalizing the new factors?
- Other questions proposed by SC members?

# Next SC Meeting

- The next meeting will take place in October.
- PMPRB staff will respond to feedback received from members in the interim.
- Members will review case studies presented by PMPRB staff and discuss the sequencing of the new regime relative to CADTH and pCPA processes.
- SC members are invited to provide feedback (by September 21) to identify specific issues within the context of the proposed framework that should be explored in case studies.

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# Guideline Modernization Case Studies

December 13th, 2018

Canada

# Summary of Cases

| | Treatment cost (annual or full regimen) | Potential treatment population (annual) | Potential annual revenues | Profile | Potential disease area |
|---|---|---|---|---|---|
| Case 1 | $1K | 500,000 | $500M | Treats a chronic condition<br>One approved indication<br>Has comparators<br>Very large treatment population | Diabetes,<br>Mental health disorders |
| Case 2 | $7K | 100,000 | $700M | Treats a chronic condition<br>One approved indication<br>Substantial therapeutic benefit, no approved comparators<br>Large treatment population each year | AMD |
| Case 3 | $20K | 103,000 | $2B | Substantial therapeutic benefit to a less common chronic condition with a small treatment population<br>Moderate therapeutic benefit to a more common chronic condition with a large treatment population | DMARDs |
| Case 4 | $50K | 3,000 | $150M | One approved indication for 2nd line treatment of cancer<br>Several therapeutic alternatives exist<br>Small treatment population | Oncology |
| Case 5 | $50K | 200,000<br>(31,000) | $1.5B | Provides cure for a serious condition<br>Large treatment population<br>If no rationing, all could be treated in 7 years | Hep C |
| Case 6 | $300K | 1,000 | $300M | Rare disease drug with one indication<br>Limited clinical significance<br>Small treatment population, high severity of illness, unmet need | EDRD |

# Acronyms

HIPC – Highest international price comparison

MIPC –Median international price comparison

LIPC – Lowest international price comparison

TCC – Therapeutic class comparison

MLP – Maximum list price

MAPP – Maximum average potential price

MRP – Maximum rebated price

NEAP – Non-excessive average price

HTA – Health Technology Assessment

QALY – Quality-adjusted life year gained

ICER – Incremental cost-effectiveness ratio

PV – pharmacoeconomic value

$/QALY – cost per quality adjusted life years gained

RWE – Real world evidence

# Case 1 – Large population, therapeutic comparators

- Treats a chronic condition
- Has therapeutic comparators
- One approved indication by Health Canada (HC)
- Very large potential treatment population
  - Possible indications: diabetes, mental health disorders, etc.
- Annual treatment cost (list price): $1,000*
- Population with the condition: 500,000
- Potential annual revenues based on the total treatment population: $500M
- Category 1 due to market size

* Assumed a once-a-year dose for ease of calculations.

# Case 1 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $800 | $785 | $780 | $750 | $750 | $750 | $750 |
| PV Threshold Price** | N/A | $640 | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $33M | $50M | $68M | $75M | $81M | $91M |
| Market Size Adjustment *** | N/A | N/A | 10% | 30% | N/A | N/A | N/A |
| MRP | N/A | $640 | $627 | $581 | $581 | $581 | $581 |
| Total revenue at MRP | N/A | $33M | $49M | $61M | $68M | $74M | $82M |

*MLP/MRP frozen.
**CADTH estimated ICER is $100K. PV threshold used is $60,000/QALY.
***A progressive discount applies to the total annual drug cost (revenue) at the cost-effective price, where each successive $10M above $40M is discounted by an additional 10%, up to a maximum of 50%. This $40M market size threshold has been used for demonstration purposes only.

# Case 1 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$1,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $1900 (assume top of TCC > MIPC) | Ex-factory price ceiling (MLP): $750<br><br>Rebated price ceiling (MRP): (frozen at year 3): $581 |
| Tests used to set the Ceiling | Midpoint of top of TCC and MIPC (moderate improvement) | MLP: MIPC<br>MRP: 30% adjustment to PV price |
| Ceiling percent reduction from original price | none | MLP: 25%<br>MRP: 42% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 2 – Large population, no therapeutic alternatives

- Treats a chronic condition
- One clinically significant approved indication
- No therapeutic alternatives
- Large treatment population
  - Potential disease areas: age-related macular degeneration (AMD).
- Annual treatment cost (list price): $7K
- Population with the condition: 100K in any given year
- Potential annual revenues based on the total treatment population: $700M
- Category 1 based on projected market size, no therapeutic alternatives

# Case 2 –Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 |
|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $6.7K | $6.3K | $6.0K | $6.0K | $6.0K | $6.0K |
| PV Threshold Price** | N/A | $3,490 | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $67M | $97M | $125M | $80M | $97M |
| Market Size Adjustment | N/A | 30% | 50% | N/A | N/A | N/A |
| MRP | N/A | $3,050 | $2,525 | $2,525 | $2,525 | $2,525 |
| Total Revenue at MRP | N/A | $62M | $79M | $92M | $70M | $79M |

*MLP/MRP frozen at year 3.
**CADTH estimated ICER is $100K. PV threshold used is $60K/QALY.

# Case 2 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$7,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $6000 | Ex-factory price ceiling (MLP): $6000<br><br>Rebated price ceiling (MRP): $2525 |
| Tests used to set the Ceiling | MIPC | MLP: MIPC<br>MRP: cost effectiveness adjusted for market size |
| Ceiling percent reduction from original price | 14% | MLP: 14%<br>MRP: 64% |
| Compliance assessment made against | ATP (rebated price, rebates include free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 3 – Two indications with different therapeutic benefits and prevalence rates

- Treats 2 chronic conditions
  - Condition 1 (first indication): estimated 3,000 people in Canada, first in class, brings significant therapeutic improvement over standard of care
  - Condition 2 (subsequent indication): Estimated 100,000 people in Canada, Therapeutic alternatives available, brings slight or no therapeutic improvement
- No therapeutic alternatives for condition 1, therapeutic alternatives for condition 2
- Annual treatment cost: $20K
- Potential annual revenues based on the total treatment population: $2B
- Category 1 based on projected market size.

# Case 3 – Application of the Proposed Guidelines (first indication)

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $19K | $18K | $17K | $17K | $17K | $17K | $17K |
| PV Threshold Price *** | N/A | $9,975 | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $99M | $143M | $195M | $249M | $304M | $362M |
| Market Size Adjustment | N/A | 40% | 50% | 50% | N/A | N/A | N/A |
| MRP | N/A | $7,580 | $6,329 | $5,835 | $5,835 | $5,835 | $5,835 |
| Revenue at MRP | N/A | $80M | $102M | $128M | $163M | $199M | $237M |

*MLP frozen based on 7 countries.
**MRP frozen after 3 years.
*** ICER threshold used is $60K/QALY.

# Case 3 – Application of the Proposed Guidelines (second indication)

Several therapeutic resulting in median TCC $6,000; LIPC = $14K

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MIPC | $19K | $18K | $17K | $17K | $17K | $17K | $17K |
| PV Threshold Price *** | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| MLP=higher of LIPC and median TCC | $14K | $13 | $12.5 | $12.5 | $12.5 | $12.5 | $12.5 |
| Revenue at MLP | $72M | $137M | $201M | $237M | $348M | $426M | $507M |
| Market Size Adjustment | N/A | 20% | 30% | 40% | N/A | N/A | N/A |
| MRP | $6,000 | $5,627 | $4,680 | $3,712 | $3,712 | $3,712 | $3,712 |
| Revenue at MRP | $31M | $59M | $75M | $81M | $103M | $126M | $151M |

# Case 3 –Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$20,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling Indication 1 | $19,000 | Ex-factory price ceiling (MLP): $17,000<br><br>Rebated price ceiling (MRP): $7,580 |
| Price Ceiling Indication 2 | $19,000 | Ex-factory price ceiling (MLP): $14,000<br><br>Rebated Price ceiling (MRP): $5,627 |
| Tests used to set the Ceiling | MIPC | MLP: MIPC for condition 1<br>LIPC for condition 2<br>MRP: lower of MLP or med TCC adjusted for market size for condition 2 |
| Ceiling percent reduction from original price | None | MLP: 10%; 26%<br>MRP: 60%; 70% |
| Compliance assessment made against | ATP (rebated price, rebates include free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 4 – 2nd line oncology medicine

- One clinically significant approved indication
- Several therapeutic alternatives exist
- Low 5-year survival rates
- Small treatment population: 3,000
- Annual treatment cost: $50,000
- Potential annual revenues based on the total treatment population: $150M
- Category 1 based on projected market size, annual treatment cost above GDP/capita

# Case 4 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $47.5K | $45K | $42.5K | $40K | $40K | $40K | $40K |
| PV Threshold Price** | N/A | $25K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $10M | $15M | $19M | $25M | $30M | $36M |
| Market Size Adjustment*** | N/A | MIPC | MIPC | MIPC | MIPC | MIPC | MIPC |
| MRP | N/A | $45K | $42.5K | $40K | $40K | $40K | $40K |
| Revenue at MRP | N/A | $14M | $20M | $26M | $33M | $40M | $47M |

*MLP/MRP frozen.
**CADTH estimated ICER is $250K. PV threshold used is $60K/QALY.
***Positive market size adjustment owing to small market size – lower of MIPC, 2xPV Threshold price

# Case 4 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$50,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $45K (assume top of TCC < MIPC) | Ex-factory price ceiling (MLP): $40K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $40K |
| Tests used to set the Ceiling | Midpoint of top of TCC and MIPC (moderate improvement) | MLP: MIPC<br>MRP: Lower of MIPC, 2xPV threshold price |
| Ceiling percent reduction from original price | 10% | MLP: 20%<br>MRP: 20% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 5 – Curable condition, large treatment population

- Provides cure for a common and serious condition
- Large treatment population: estimated 200,000 Canadians are living with the condition
  - All could be treated in seven years assuming no rationing
- As of 2018, the health care system cost associated with the condition is estimated at $10 billion annually.
- Annual treatment cost of $50K (based on the manufacturer's suggested list price)
- Potential annual revenues based on the total treatment population: $1.5B
- Category 1 based on projected market size, annual treatment cost above GDP/capita

# Case 5 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $48K | $45K | $43K | $43K | $43K | $43K | $43K |
| PV Threshold Price*** | N/A | $50K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $1.5B | $1.5B | $1.5B | $1.5B | $1.5B | $1.5B |
| Market Size Adjustment**** | N/A | 50% | 50% | 50% | 50% | 50% | 50% |
| MRP | N/A | $25K | $24K | $23K | $23K | $23K | $23K |
| Total revenue at MRP | N/A | $770M | $740M | $708M | $708M | $708M | $708M |

*MLP frozen based on 7 countries.
**MRP frozen.
***CADTH estimated ICER is $50K, below PMPRB PV threshold
****Maximum market size adjustment of 50%. Assuming competitor entry in Year 6.

# Case 5 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$50,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $48K (assume top of TCC < MIPC) | Ex-factory price ceiling (MLP): $43K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $25K |
| Tests used to set the Ceiling | Higher of top of TCC and MIPC (substantial improvement) | MLP: MIPC<br>MRP: 50% adjustment to PV price |
| Ceiling percent reduction from original price | 4% | MLP: 14%<br>MRP: 50% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 6 – Rare disease drug

- Rare disease drug with one indication
- Limited clinical significance (moderate improvement over placebo) but offers hope for the first time for a severe condition with high burden of illness and high unmet need.
- Small treatment population: 1,000 Canadians diagnosed with the condition, 2% increase per year.
  - One in every 4,000 children born are affected by the condition.
- Annual treatment cost: $300,000
- Potential annual revenues based on the total treatment population: $300M
- Category 1 based on projected market size, annual treatment cost above GDP/capita

# Case 6 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $240K | $240K | $240K | $240K | $240K | $240K | $240K |
| PV Threshold Price** | N/A | $60K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $60M | $61M | $62M | $64M | $65M | $66M |
| Market Size Adjustment*** | N/A | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV |
| MRP | N/A | $120K | $120K | $120K | $120K | $120K | $120K |
| Total revenue at MRP | N/A | $30M | $30.5M | $31M | $32M | $32.5M | $33M |

*MLP/MRP frozen.
**CADTH estimated ICER is $300K-700K, depending on population and severity. Assume 80% price reduction required to meet PMPRB PV threshold of $60K/QALY.
***Positive market size adjustment owing to small market size – lower of MIPC, 2xPV Threshold price.

# Case 6 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$300,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $240K | Ex-factory price ceiling (MLP): $240K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $120 |
| Tests used to set the Ceiling | Midpoint of top of TCC and MIPC (moderate improvement, no comparators) | MLP: MIPC<br>MRP: 2xPV price |
| Ceiling percent reduction from original price | 20% | MLP: 20%<br>MRP: 60% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

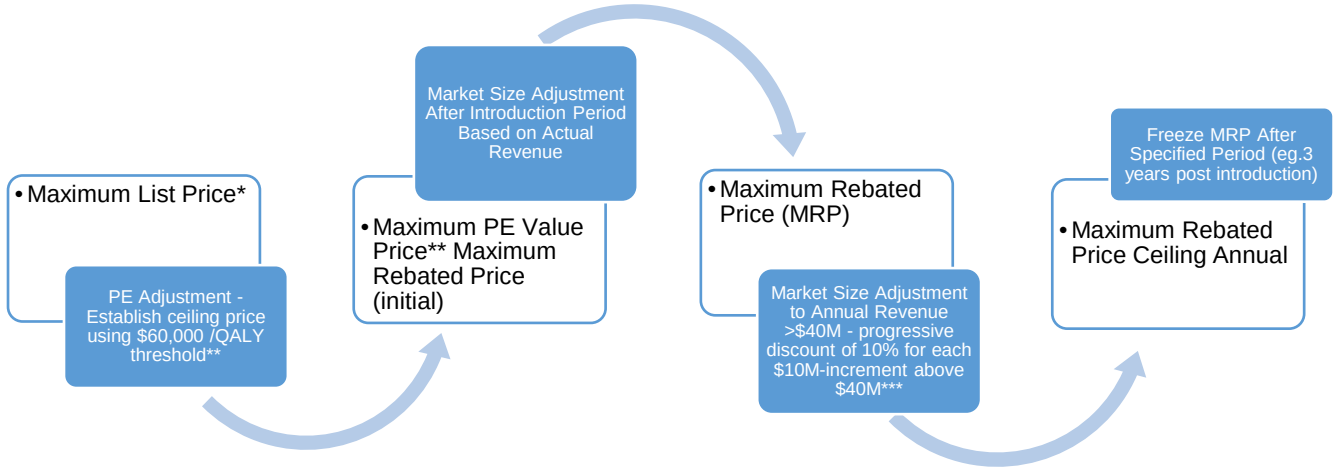
# PMPRB Framework Modernization
# Proposed Application of PE and Market Size Factors to Category 1 Drugs

*Disclaimer*

*This document is not to be viewed as a definitive interpretation of the current or proposed legislation or of the RIAS for the proposed amendments by the PMPRB, is not the Government's expression of policy intent or an official part of the consultation, and is not intended to bind the PMRPB or the Government in the application and interpretation of legislation.*

Category 1 drugs are very expensive, new, patented drugs that are an effective treatment for a life threatening and/or debilitating disease. Under the proposed new guidelines, the PMPRB will assign two distinct price ceilings to each Category 1 drug[1] – the Maximum List Price (MLP) and the Maximum Rebated Price (MRP). The factors related to pharmacoeconomic (PE) value and market size will be applied, in that order, to set the MRP[2] for a Category 1 drug. The way in which each of the factors will be applied to render the MRP of a Category 1 drug is described in figures 1 and 2. These figures demonstrate approaches to getting to an MRP ceiling that involves a decrease from the PE value price (large market size) or an increase from the maximum PE value price (small market size e.g. orphan drugs).

**Figure 1. Getting to MRP for Category 1 Drugs (Non-Orphan)**




* **The Maximum List Price (MLP)** is the lower amount generated by the median international price comparison (MIPC) test or the therapeutic class comparison (TCC) test. This test applies to any new drug (Category 1 and Category 2).

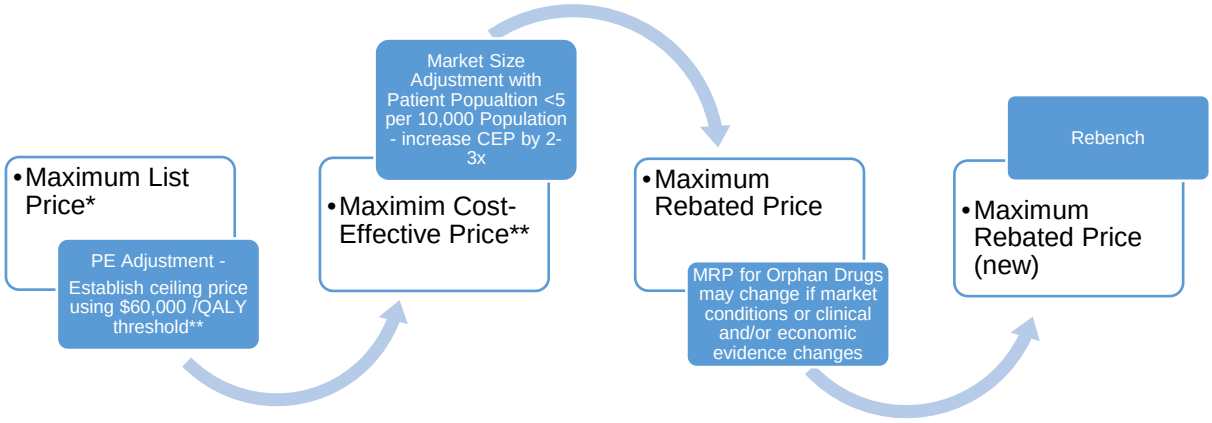
** **The Pharmacoeconomic (PE) Value Price** is the maximum treatment cost under a set cost per quality-adjusted life year gained ($/QALY) threshold. Best available evidence for Canada suggests that the health care system is currently paying $30,000 to purchase an additional QALY. This implies that a drug whose incremental cost-effectiveness ratio (ICER) exceeds this threshold would generate a net health loss. In order to apply this evidence in the national PMPRB context, setting the baseline $/QALY threshold at two-times that amount ($60,000) is proposed.

[1] The determination of a high-cost drug involves the assessment of whether the average treatment cost is greater than per capita GDP. For example, high-cost could represent any drug with an average (annual or appropriate regiment) treatment cost of $50,000 or more.

[2] The Maximum Rebated Price (MRP) is also described as the maximum reimbursement price. In contrast to the maximum listed price (MLP) which is public, the MRP is confidential and is assessed against average prices that include rebates to institutional payers (provincial drug plans and large private insurers).

***The Market Size Adjustment** for high-impact drugs is based on the annual reported revenues after the initial year. Adjustment to the PE value price ceiling to get to the MRP would reflect annual sales surpassing $40M.[3] The reduction in MRP involves a progressive discounting methodology. The progressive discount applies to the total annual drug cost where each successive $10M above $40M is discounted by an additional 10%, up to a maximum of 50%. Conversely, market size may be used to increase the ceiling for medicines with small market sizes such as rare diseases. In general, the practice is to adjust the value of the ICER, however, the approach that is being proposed by the PMPRB would use the same baseline ICER threshold, but adjust the final price ceiling up or down taking market size into consideration. The MRP could be adjusted upwards by as much as two to three times depending on the drug and other considerations or modifiers as discussed previously (e.g. drugs for rare disorders).

**Figure 2. Getting to MRP for Category 1 Orphan Drugs**




[3] The example uses $40M as the large market size trigger, however within the Canadian context $20M would signal affordability challenges for the health care system based on the recent years of GDP growth.

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# Steering Committee Consultation Roadmap - Update

Canada

# Review of Meetings

First meeting (June 25, 2018)

1. Background on Guidelines Reform
2. Objectives and guiding principles
3. Outline of proposed new Guidelines framework and associated suggested questions

# Review of Meetings

Second - teleconference calls (August 15, 2018)

- Use of external price referencing
- Use of List and Net price ceilings
- Risk assessment and prioritization criteria for Category 1 and 2 drugs
- Re-benching criteria

# Review of Meetings

Third Meeting- teleconference calls (September 12, 2018)

1. Tests for Category 1 drugs
2. Tests for Category 2 drugs
3. Use of confidential pricing information
4. Application of new regime to existing drugs

# Review of Meetings

December 13, 2018 – face to face meeting

Case Studies

1. Large size market with therapeutic alternatives
2. Large size market with no therapeutic alternatives
3. Two indications with different market conditions
4. Second line oncology
5. Cure for large population
6. EDRD drug

# Next Steps

- Final Report of Technical Working Group – Feb/2019
- PMPRB Solicit final written feedback from SC Feb/2019
  - Specific questions on each topic and on proposed framework overall
- PMPRB distribute draft SC Report to members 2 weeks prior to final meeting
- Final face-to-face meeting to review the draft report and finalize
- Final SC and TWG reports submitted to the Board
- Release Draft Guidelines for next phase of consultation post CG2

# Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines

# **Final Report**

March 2019

# Contents

# Purpose

The purpose of this report is to summarise the deliberations and recommendations of the Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines.

# Introduction

In June 2018, the PMPRB established a *Steering Committee on Modernization of Price Review Process Guidelines* (hereafter the 'Steering Committee'). Its mandate was to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of the PMPRB's new draft Guidelines.

In July 2018, the PMPRB established the *Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines* (hereafter the 'Working Group'). Its mandate was to inform the Steering Committee on certain issues that the Steering Committee believed would benefit from the review of experts in health technology assessment and other economic and scientific matters.

This report provides a summary of the Working Group's deliberations and recommendations.

## Membership

The chair of the Working Group was Dr Mike Paulden (University of Alberta).

Twelve individuals sat as members of the Working Group (listed alphabetically):

1. Sylvie Bouchard (INESSS)[1] [represented by Patrick Dufort and Marie-Claude Aubin];
2. Dr Chris Cameron (Dalhousie University and Cornerstone Research Group);
3. Dr Doug Coyle (University of Ottawa);
4. Don Husereau (University of Ottawa);
5. Dr Peter Jamieson (University of Calgary);
6. Dr Frédéric Lavoie (Pfizer Canada) (*Industry Representative*);
7. Karen Lee (University of Ottawa and CADTH)[2];
8. Dr Christopher McCabe (University of Alberta and Institute of Health Economics);
9. Dr Stuart Peacock (Simon Fraser University and BC Cancer Agency);
10. Maureen Smith (*Patient*);
11. Geoff Sprang (Agmen) (*Industry Representative*);
12. Dr Tania Stafinski (University of Alberta).

Two individuals sat as observers of the Working Group:

1. Edward Burrows (Innovation, Science and Economic Development);
2. Nelson Millar (Health Canada).

One individual acted as an external reviewer of the Working Group's draft report:

1. Dr Mark Sculpher (University of York).

An additional individual from CADTH, Dr Tammy Clifford, accepted an invitation to sit as a member of the Working Group but did not participate in the Working Group's deliberations. Dr Clifford also did not contribute towards, or vote on, the Working Group's recommendations.

[1] INESSS: Institut national d'excellence en santé et services sociaux
[2] CADTH: Canadian Agency for Drugs and Technologies in Health

# Terms of Reference

The Terms of Reference (Appendix 4) required that the Working Group examine and make recommendations with respect to specific considerations and questions within the following six 'areas of focus':

1. ***Options for determining what medicines fall into 'Category 1'***

    - *A Category 1 medicine is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing.*
    - *The following criteria have been identified as supporting a Category 1 classification:*
        A. *The medicine is 'first in class' or a 'substantial' improvement over existing options*
        B. *The medicine's opportunity cost exceeds its expected health gain*
        C. *The medicine is expected to have a high market impact*
        D. *The medicine has a high average annual treatment cost*
    - *Should other criteria be considered? What are the relevant metrics for selecting medicines that meet the identified criteria and what options exist for using these metrics?*

2. ***Application of supply-side cost effectiveness thresholds in setting ceiling prices for Category 1 medicines***

    - *Potential approaches for implementing a price ceiling based on a medicine's opportunity cost.*
    - *Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc)*

3. ***Medicines with multiple indications***

    - *Options for addressing medicines with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).*

4. ***Accounting for uncertainty***

    - *Options for using the CADTH and/or INESSS reference case analyses to set a ceiling price.*
    - *Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.*

5. ***Perspectives***

    - *Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a 'significant' difference between price ceilings under each perspective.*
    - *How to define a 'significant' difference in price ceilings between each perspective.*

6. ***Application of the market size factor in setting ceiling prices***

    - *Approaches to derive an appropriate affordability adjustment to a medicine's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' [Institute for Clinical and Economic Review] approach).*

Under the Terms of Reference, the Steering Committee had the opportunity to specify additional areas of focus for the Working Group. The Steering Committee did not identify any additional areas of focus for the Working Group to consider.

## Objections

The industry members (Frédéric Lavoie and Geoff Sprang) repeatedly raised objections to what they regarded as the *"very narrow boundaries"* established by the Terms of Reference.

Among these objections was a concern that the Working Group was not permitted to examine whether the PMPRB *should* be considering economic factors as part of the proposed reforms, nor any logistical or operational issues associated with implementation of the proposed reforms.

The industry members also stated that, as representatives of BIOTECanada and Innovative Medicines Canada (IMC), they *"do not support the inclusion of proposed economic factors in a quasi-judicial price ceiling regulatory methodology given the uncertainty these factors would introduce, their practical challenges and complexity of implementation"*, arguing that *"the government's regulatory objectives can be achieved by much simpler, more transparent and predictable mechanisms that will ensure access to necessary prescription medications while achieving the regulatory "bright lines" which PMPRB has recognized as a key consideration"*.

The industry members submitted a number of 'on the record' comments to the chair regarding these and other matters, all of which are reproduced *verbatim* in Appendix 3.1 to 3.5.

The patient member (Maureen Smith) also submitted 'on the record' comments regarding these and other matters, which are reproduced *verbatim* in Appendix 3.6.

## Policy intent

The PMPRB provided the Working Group with a copy of the *Regulations Amending the Patented Medicines Regulations*, as published in Canada Gazette Part I: Vol 151 (2017). This document includes a *Regulatory Impact Analysis Statement* and the *Proposed Regulatory Text* and is reproduced in Appendix 5.1.

**The Working Group was instructed by the PMPRB to make its considerations and recommendations on the assumption that the Regulations Amending the Patented Medicines Regulations will remain unchanged in their final publication.**

The Working Group therefore considered the Regulatory Impact Analysis Statement and Proposed Regulatory Text as providing a definitive statement of the policy intent with respect to the proposed regulations.

In addition, the PMPRB provided three supporting documents to aid the Working Group in understanding the policy intent:

1. PMPRB Guidelines Scoping Paper (Appendix 5.2);
2. PMPRB Framework Modernization Presentation (Appendix 5.3);
3. PMPRB Short Primer (Appendix 5.4).

The chair sought clarity from the PMPRB in cases where the Working Group was not clear about any aspect of the policy intent.

## Process and procedure

The Working Group was convened in July 2018 and met three times in-person and multiple times via teleconference between July 2018 and February 2019:

1. 26 July 2018 (all day in-person meeting);
2. 22 and 24 August 2018 (1 hour teleconference for each of six areas of focus);
3. 24 August 2018 (2 hour teleconference);
4. 25 September 2018 (2 hour teleconference);
5. 12 October 2018 (all day in-person meeting);
6. 28 November 2018 (2 hour teleconference);
7. 5 February 2019 (all day in-person meeting).

The Working Group was originally intended to report in October 2018, but this timeline was extended until March 2019.

Detailed meeting notes were taken by PMPRB staff and emailed to the chair following each meeting. A draft summary of these notes was circulated among Working Group members. In order to encourage a frank and open discussion, the chair committed to not identifying members alongside their comments in the Working Group's report, unless requested to by the member. Members were permitted to provide 'on the record' comments regarding any matters of concern.

One week prior to the final in-person meeting on 5 February 2019, the chair circulated a draft 'Conceptual Framework' to all members. A revised version is reproduced in Appendix 1.
The purpose of this 'Conceptual Framework' was to guide members in making consistent recommendations across all six areas of focus, while respecting the policy intent and the range of views expressed by members throughout the Working Group's deliberations.

On 7 February 2019, the chair circulated a set of 'draft potential recommendations'. Members were invited to submit comments or suggested modifications until 15 February 2019.

On 18 February 2019, the chair circulated a draft report of the Working Group's deliberations to all members and the external reviewer, including a final set of 'potential recommendations'.

Under the Terms of Reference, recommendations were determined by a vote of the members, with the chair having the casting vote in the event of a tie. Members were asked to vote on the potential recommendations using an online form, and the full results of the vote were shared with all members. The chair committed not to identify members who voted 'in favour' or 'against' each potential recommendation in the Working Group's final report.

Comments on the draft report, and votes on the potential recommendations, were accepted until 1 March 2019. The final report was submitted to the PMPRB on 6 March 2019.

# 1: Criteria for classifying medicines as ‘Category 1’

## 1.1 Terms of Reference

Within this area of focus, the Terms of Reference required the Working Group to examine and make recommendations with respect to the following considerations and questions:

*A Category 1 medicine is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing.*

*The following criteria have been identified as supporting a Category 1 classification:*

A. *The medicine is ‘first in class’ or a ‘substantial’ improvement over existing options;*
B. *The medicine’s opportunity cost exceeds its expected health gain;*
C. *The medicine is expected to have a high market impact;*
D. *The medicine has a high average annual treatment cost.*

*Should other criteria be considered? What are the relevant metrics for selecting medicines that meet the identified criteria and what options exist for using these metrics?*

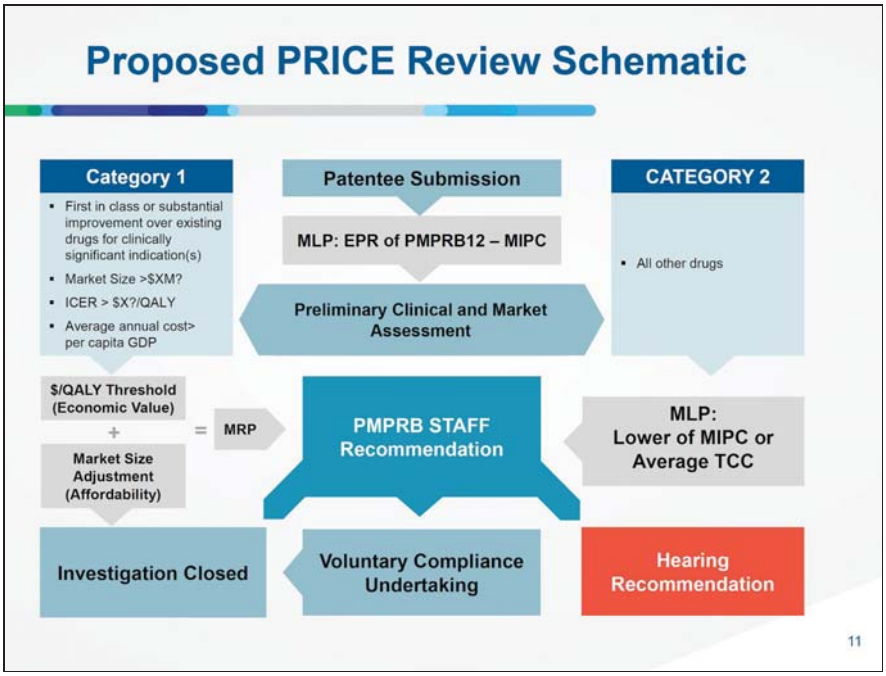
The chair clarified with the PMPRB whether the Terms of Reference permitted the Working Group to consider whether any of the criteria should be *omitted*. The PMPRB confirmed that such a consideration was within the purview of the Working Group.

## 1.2 Policy Intent

The PMPRB Guidelines Scoping Paper includes the following statement which provides context regarding the policy intent with respect to this area of focus:

> *"The second part of the framework consists of a screening phase which would* ***classify new patented drugs as either high or low priority*** *based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans). At this stage in the process, the PMPRB would consider whether the drug is* ***first in class,*** *has* ***few or no therapeutic alternatives,*** *provides* ***significant therapeutic improvement over existing treatment options,*** *is* ***indicated for a condition that has a high prevalence in Canada,*** *is a* ***high cost drug*** *(i.e. an average annual cost higher than a GDP-based threshold) or is* ***classified as a high priority drug by other agencies/regulators in the health care system*** *(such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or Health Canada) because of* ***unmet medical need****. Drugs that appear to be* ***high priority*** *based on these screening factors would be subject to* ***automatic investigation and a comprehensive review*** *to determine whether their price is potentially excessive."*
>
> *(p.6,* ***emphasis added****)*

The PMPRB Framework Modernization Presentation includes the following slide which provides context regarding the policy intent with respect to this area of focus:



## 1.3 Summary of Deliberations

There was widespread agreement among members of the Working Group that not all medicines require the same extent of review, and that a 'risk-based' approach is desirable.

However, there was debate among the Working Group regarding the criteria that should be used by the PMPRB to identify medicines at elevated risk of excessive pricing ('Category 1').

### 1.3.1 No other criteria considered

Under the Terms of Reference, the Working Group was required to examine and make recommendations regarding whether "other criteria" should be considered by the PMPRB.

No members of the Working Group proposed that any other criteria be considered beyond those specified in the Terms of Reference.

The following *potential* recommendation was put to a vote of the Working Group:

***1.1: The Working Group does not recommend any additional criteria beyond those specified in the Terms of Reference.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.2 'Substantial improvement over existing options'

A number of members expressed concern about the wording of Criterion A (*'The medicine is 'first in class' or a 'substantial' improvement over existing options'*).

Although there was general agreement that 'first in class' medicines should be classified as 'Category 1', many members questioned why medicines that offer *"a 'substantial' improvement over existing options"* should be classified as 'Category 1' if none of the other criteria are met.

Concern was raised by some members that inclusion of this term might penalize manufacturers for producing medicines that offer 'substantial improvement', disincentivizing their development. Some members questioned whether this would, in turn, undermine the policy intent.

The chair asked the PMPRB to clarify the policy intent behind the inclusion of this term. The PMPRB responded that medicines that offer a 'substantial' improvement over existing options are more likely to dominate their respective market, increasing the risk of 'excessive pricing'.

Some members argued that, even if a medicine dominates its market, if the medicine does not have 'high' market impact or a 'high' average annual treatment cost then the number of patients affected will be relatively small. Within a 'risk based' approach to classifying medicines, this might justify excluding the 'substantial improvement' term from Criteria A. One member dissented from this position, arguing that the PMPRB has a mandate to protect consumers from 'excessive prices', even if the number of patients affected is small.

Members of the Working Group were unable to identify examples of medicines which offer a 'substantial' improvement over existing options but would *not* be considered 'first in class' and would *not* have 'high' market impact or a 'high' average annual treatment cost. Even if inclusion of the 'substantial improvement' term is consistent with the policy objective, this raises the question as to whether its inclusion is redundant, given the presence of these other criteria.

The following *potential* recommendation was put to a vote of the Working Group:

***1.2: The Working Group recommends that the PMPRB consider whether the wording "substantial improvement over existing options" within Criterion A is redundant or inconsistent with the policy intent, and, if so, remove this from consideration.***

Members voted **11 in favour** and **1 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.3 'Opportunity cost' criterion

There was widespread agreement that Criterion B ('*The medicine's opportunity cost exceeds its expected health gain'*) should not be considered when classifying medicines as 'Category 1'.

Some members cited the logistical difficulty of establishing cost-utility estimates for all newly launched medicines, rather than only those classified as Category 1. However, since logistical issues were not within scope of the Terms of Reference, these issues were not considered by the Working Group.

The industry members argued that the PMPRB's proposed $30,000 per quality-adjusted life year (QALY) threshold is sufficiently low as to capture over 90% of all new medicines, such that classification as 'Category 1' would not serve as a useful screening mechanism. A potential response to this specific concern would be to raise the threshold used for screening to a sufficiently high level that a manageable number of new medicines are classified 'Category 1'.

Another reason for excluding Criterion B, given by some members and consistent with the Conceptual Framework, is that this criterion may be redundant in the presence of the other criteria. If a medicine does not satisfy *any* of the other criteria - that is, it does not have a 'high' average annual cost, does not have 'high' market impact, is not 'first in class' and does not offer a 'substantial improvement' over existing treatment - then the potential loss in consumer surplus that might result from its adoption is limited, regardless of the incremental cost-effectiveness ratio (ICER). Under a risk-based approach, it may therefore be better to focus the resources available for assessing 'Category 1' medicines on medicines with 'high' average annual treatment cost, 'high' market impact and/or the potential to dominate their respective market.

The following *potential* recommendation was put to a vote of the Working Group:

***1.3: The Working Group recommends that Criterion B be removed from consideration.***

Members voted **11 in favour** and **1 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.4 'High average annual treatment cost'

There was disagreement amongst the Working Group regarding Criterion D ('*The medicine has a high average annual treatment cost*'), specifically whether 'high average annual treatment cost' should be considered in absolute terms or as *incremental* upon existing treatment.

It was noted that a new medicine could have 'high average annual treatment cost', but might replace an existing treatment that *also* has 'high average annual treatment cost', such that the *incremental* average annual treatment cost is not 'high'.

Some members noted that, if the *existing* treatment has 'high average annual treatment cost', this increases the risk that the existing treatment is itself considered to be 'excessively priced'. In such cases, the new medicine may also be considered to be 'excessively priced', even if the *incremental* average annual treatment cost is not 'high'.

As noted in the Conceptual Framework, the opportunity cost of adopting a new medicine is a function of its *incremental* cost compared to existing treatment. All else equal, the risk that adopting a new medicine will result in negative consumer surplus would therefore be expected to be greater for a medicine with high *incremental* average annual treatment cost, compared to a medicine with high *absolute* average annual treatment cost but low *incremental* average annual treatment cost. For this reason, the PMPRB may wish to consider 'average annual treatment cost' within Criterion D as being *incremental* upon existing treatment.

There are several considerations that would need to be be made when calculating this incremental cost. The relevant treatment comparator would need to be established and the cost of treatment with the comparator estimated over the relevant time horizon. If the comparator is itself a patented medicine, then consideration would also need to be given to any expected reduction in the cost of the comparator should generic alternatives to the comparator become available during the patent life of the new medicine.

The following *potential* recommendation was put to a vote of the Working Group:

***1.4: The Working Group recommends that "average annual treatment cost" within Criterion D be considered as incremental upon existing treatment.***

Members voted **11 in favour** and **1 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.5 Relevant metrics

The Terms of Reference required that the Working Group examine and make recommendations regarding the *"relevant metrics for selecting medicines that meet the identified criteria"*.
The chair interpreted this as referring to the measures and definitions used for each criteria. For example, if the term 'substantial improvement' is retained in Criterion A, how would 'improvement' be measured and how would a 'substantial improvement' be defined?

There was general agreement that the most appropriate metrics for each criterion would be those already used in Canadian practice. For example, if the PMPRB retains consideration of the 'substantial improvement' term in Criterion A, then the definition of 'substantial improvement' could be based upon the definition already adopted by the PMPRB. Other potential sources for definitions suggested by members included health technology assessment (HTA) and regulatory agencies in Canada.

The following *potential* recommendation was put to a vote of the Working Group:

***1.5: The Working Group recommends that the measures and definitions used for each criterion reflect existing Canadian practice.***

Members voted **10 in favour** and **2 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.6 Determining a threshold for each criterion

In addition to identifying "relevant metrics", the Terms of Reference required that the Working Group examine and make recommendations regarding "options" for using these metrics.

There was some discussion regarding how to determine an appropriate 'threshold' to adopt for each criterion, building upon some potential thresholds proposed by the PMPRB.

At the first meeting of the Working Group, the PMPRB proposed that, in considering Criterion B ('*The medicine's opportunity cost exceeds its expected health gain*'), the ICER could potentially be compared to a threshold of $30,000 per quality-adjusted life year (QALY). This was based on an estimate by Ochalek *et al.* (2018) of the opportunity cost of funding new medicines within Canada's public health care systems (considered further in Topic 2).[1] Some members raised concern that a $30,000 per QALY threshold would be sufficiently low as to capture a substantial proportion of all new medicines considered by the PMPRB, such that categorization as 'Category 1' might not serve as a useful 'screening' mechanism. However, in light of the general consensus among the Working Group that Criterion B should not be considered by the PMPRB, no further discussion of this threshold took place.

The PMPRB also proposed a potential 'market impact' threshold of either $20m or $40m, and proposed that a medicine could be considered to be of 'high market impact' if it reached this threshold in any one of either the first 3 years or 5 years after launch. The PMPRB provided the Working Group with estimates of the proportion of all medicines that would be classified as 'Category 1' under each combination of these potential thresholds (based solely on Criterion C):

- $20m market size in any one of the first 3 years: 22% of all medicines
- $20m market size in any one of the first 5 years: 27% of all medicines
- $40m market size in any one of the first 3 years: 17% of all medicines
- $40m market size in any one of the first 5 years: 20% of all medicines

Finally, the PMPRB proposed a potential 'average annual treatment cost' threshold of $50,000. The PMPRB estimated that this threshold would result in 4% of all medicines being classified as 'Category 1' (based solely on Criterion D).

The Working Group noted that the sensitivity of each criterion as a 'screen' is dependent upon the threshold adopted. The Working Group did not have the necessary data to calculate how many medicines would be classified as 'Category 1' under different combinations of thresholds across the criteria. Furthermore, it was noted that the 'ideal' number of medicines to classify as 'high risk' depends upon the PMPRB's capacity for assessing 'Category 1' medicines (which was unknown to the Working Group), while the 'ideal' types of medicines to classify as 'high risk' depend upon the policy intent.

The Working Group was therefore not in a position to make specific recommendations regarding the threshold to adopt for each criterion. Instead, the chair proposed that the PMPRB should determine the threshold for each criterion, taking into account its capacity for assessing 'Category 1' medicines, the technical considerations of the Working Group, and the policy intent.

The following *potential* recommendation was put to a vote of the Working Group:

***1.6: The Working Group recommends that a threshold for each criterion be determined by the PMPRB, taking into account its capacity for assessing 'Category 1' medicines, the technical considerations of the Working Group, and the policy intent.***

Members voted **10 in favour** and **2 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.7 Clear specification of the threshold for each criterion

The two industry members on the Working Group emphasized the importance of the PMPRB clearly specifying the threshold to be used for each criterion, so as to provide a “clear bright line” to manufacturers.

A technical justification for this request is that a clear specification of the threshold for each criterion reduces uncertainty. The Conceptual Framework outlines how uncertainty in a medicine’s pharmacoeconomic value may result in an expected loss in economic surplus, such that there may be value in reducing this uncertainty. Similarly, uncertainty in whether a medicine may be subject to ‘Category 1’ classification may impose an expected loss on manufacturers and other stakeholders.

The following *potential* recommendation was put to a vote of the Working Group:

***1.7: The Working Group recommends that the threshold for each criterion be clearly specified, so as to reduce uncertainty for stakeholders.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 1.3.8 Other considerations

There was some discussion as to whether ‘high market impact’ should be considered as *incremental* upon existing treatment (similar to the consideration of ‘high average annual treatment cost’ in section 1.3.4). Some members argued that a medicine with high market size may replace an existing treatment which also has high market size, such that the *net* market impact is relatively small.

However, it was apparent from the PMPRB Guidelines Scoping Paper, as well as the proposed ‘market size adjustment’ (section 6), that there is a policy concern regarding medicines with high *absolute* market impact. The PMPRB confirmed to the chair that this was the case. Given this policy intent, the Working Group did not consider any potential recommendation to modify the wording of the ‘high market impact’ criterion so that it is incremental upon existing treatment.

# 2: Supply-side cost effectiveness thresholds

## 2.1 Terms of Reference

Within this area of focus, the Terms of Reference required the Working Group to examine and make recommendations with respect to the following considerations and questions:

> *Potential approaches for implementing a price ceiling based on a medicine's opportunity cost.*

> *Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc).*

## 2.2 Policy Intent

The Regulatory Impact Analysis Statement includes the following statements which provide context regarding the policy intent with respect to this area of focus:

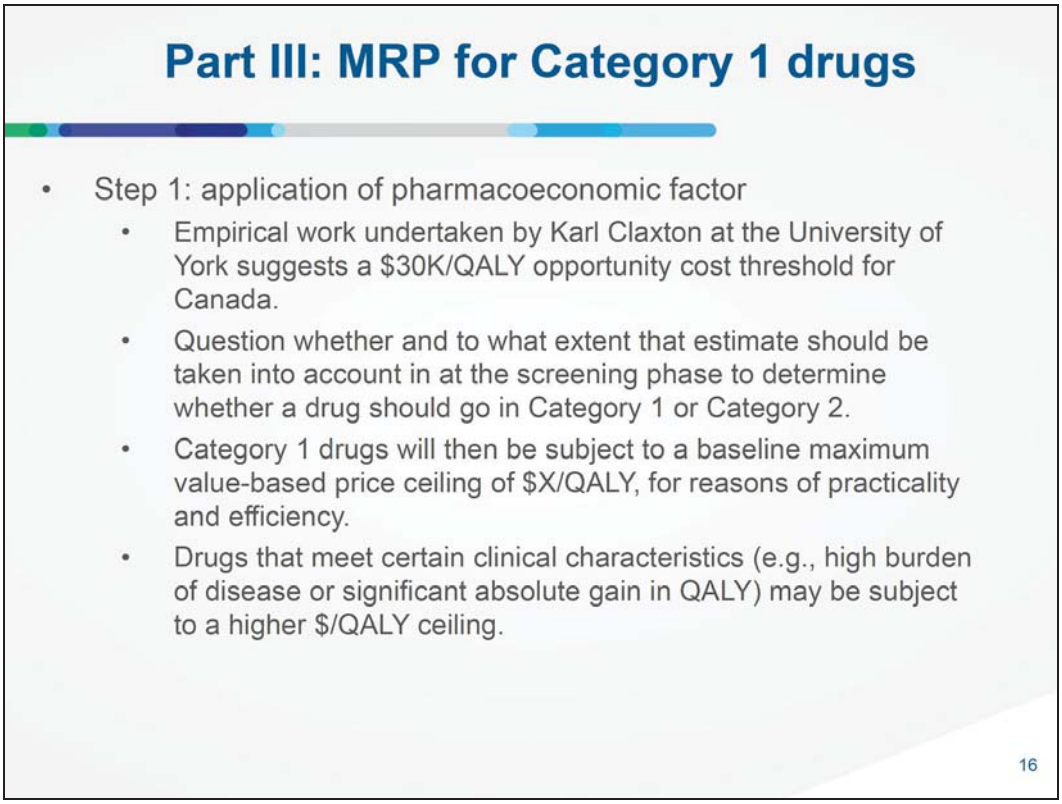
> *"Information regarding pharmacoeconomic value: patentees would be required to provide the PMPRB with all published* ***cost-utility analyses*** *that express the value in terms of the* ***cost per quality-adjusted life year (QALY)****. Cost-utility analyses are viewed by experts as the* ***"gold standard"*** *approach to considering the* ***economic value*** *of new medicines."*
>
> *(p.10,* ***emphasis added****)*

> *"Without the proposed amendments, it is estimated that* ***public health care systems from across Canada*** *will spend an additional $3.9 billion (PV) for the same quantity of patented medicine. This represents a significant* ***opportunity cost for the Canadian public health care system****, as these funds could have been used in* ***other areas of the health care system to better the health of Canadians****."*
>
> *(p.16,* ***emphasis added****)*

The PMPRB Guidelines Scoping Paper includes the following statement which provides context regarding the policy intent with respect to this area of focus:

> *"The first part of the test would* ***assess the incremental cost per quality-adjusted life year (QALY) of the drug, as determined by CADTH's health technology assessment process, against an explicit cost effectiveness threshold****. The threshold would be based on the* ***opportunity cost*** *associated with* ***displacing the least cost effective health technology in the Canadian health system****, otherwise understood as the marginal cost of a QALY, as calculated by expert health economists and* ***revised periodically to reflect changing market conditions****. Drugs that* ***prolong life or provide significant QALY gains*** *could be subject to a* ***more generous threshold****, as Canadian payers have demonstrated a* ***higher willingness to pay for these types of drugs****".*
>
> *(p.6,* ***emphasis added****)*

The PMPRB Framework Modernization Presentation includes the following slide which provides context regarding the policy intent with respect to this area of focus:



## 2.3 Summary of Deliberations

The Working Group's deliberations on this topic were informed by two documents commissioned by the PMPRB prior to establishment of the Working Group:

1. A white paper prepared by the Institute of Health Economics (IHE) titled *"Theoretical models of the cost-effectiveness threshold, value assessment, and health care system sustainability"*, hereafter referred to as the 'IHE report'.[2]
2. A report prepared by Jessica Ochalek and colleagues from the University of York titled *"Assessing health opportunity costs for the Canadian health care systems"*, hereafter referred to as 'Ochalek *et al.* (2018)'.[1]

### 2.3.1 Appropriateness of using a supply-side threshold

As noted in the IHE report, a supply-side threshold can be used to estimate the 'health opportunity cost' associated with adopting a new medicine within a public health care system. This health opportunity cost is measured in units of health benefit (typically QALYs) and reflects the estimated health 'forgone' by other patients within the health care system if limited resources are used to adopt the new medicine.

For example, Ochalek *et al.* (2018) estimated a supply-side threshold of $30,000 per QALY for Canada as a whole, with some variation across provinces and territories (considered further in section 2.3.4). This estimate implies that every additional $30,000 spent on a new medicine results in one forgone QALY by other patients across Canada's public health care systems. A higher estimate of the supply-side threshold would imply that fewer QALYs are displaced at any given incremental cost associated with a new medicine, and conversely a lower supply-side threshold would imply that more QALYs are displaced for any given incremental cost.

Additional explanation and examples are provided in the Conceptual Framework.

There was debate amongst Working Group members as to whether a supply-side threshold is always the most appropriate means for estimating the opportunity cost of new medicines. Specifically, consideration was given as to whether a 'demand-side threshold' might be more appropriate than a supply-side threshold in some cases.

As noted in the IHE report, a demand-side threshold reflects Canadians' 'willingness-to-pay' for health benefits. Some members argued that a demand-side threshold might therefore be a more appropriate threshold for private insurers and patients who pay out-of-pocket.

Nevertheless, in light of the PMPRB's clarification that the policy intent is to adopt the perspective of the Canadian public health care system (section 5.2), the focus of the Working Group's deliberations was on a supply-side approach to estimating the threshold.

Since the policy intent is to adopt the perspective of Canada's public health care systems, and since the Regulatory Impact Analysis Statement views the QALY, as used in cost-utility analysis, as the "gold standard" approach to considering the economic value of new medicines, it follows that the most relevant measure of the opportunity cost of a new medicine, given this policy intent, is an estimate of the QALYs forgone by patients within Canada's public health care systems. As noted in the Conceptual Framework, this may be estimated using an estimate of the incremental cost of the new medicine and an estimate of a supply-side cost-effective threshold, expressed in terms of cost per QALY.

The following *potential* recommendation was put to a vote of the Working Group:

***2.1: The Working Group regards the use of a supply-side cost-effectiveness threshold, as a means for estimating the opportunity cost of adopting new medicines within Canada's public health care systems, as consistent with the policy intent.***

Members voted **10 in favour** and **2 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.2 Uncertainty in the empirical evidence base

The Working Group was unanimous in considering the empirical evidence base with respect to Canadian estimates of supply-side thresholds to be uncertain.

The only existing estimate of a supply-side threshold for Canada is that provided by Ochalek *et al.* (2018). This work reported estimates of supply-side thresholds for each province and territory in terms of cost per disability adjusted life year (DALY) averted. Based on these estimates, the authors argued that *"a cost per DALY threshold is likely to be less than $50,000 for Canada as a whole"*. The authors further argued that *"a cost per QALY threshold is likely to be similar or lower than a cost per DALY averted threshold"*, concluding that *"a cost per QALY threshold of $30,000 per QALY would be a reasonable assessment of the health effects of changes in health expenditure for Canada as a whole and is likely to be similar across most provinces"*.

The authors acknowledged that this research was not primarily based upon Canadian data, noting that "*further research to provide Canadian and/or province specific elasticity estimates using within country and within province data should be regarded as a priority*".

Some members of the Working Group expressed concerns with the instrumental variables (IVs) used by Ochalek *et al.* (2018).

One member noted that the authors employed two specific IVs that are potentially problematic:

1. Military expenditure per capita of neighbouring countries;
2. A measure of institutional quality, captured using:
    a. The level of infrastructure (proxied by 'paved roads per square km');
    b. Shock in 'donor funding' (absolute deviation from the historical mean).

This member viewed the appropriateness of these IVs as questionable in the Canadian context. Canada's neighbor is the United States, which is an outlier in terms of military expenditure per capita in the sample of countries used in the Ochalek *et al.* (2018) study. Canada is also an outlier in terms of 'paved roads per square km', ranking 90th out of 125 countries.[3] Since relatively few high income countries receive 'donor funding', this member noted that 'paved roads per square km' is effectively the sole IV for infrastructure quality.

These potentially 'weak' IVs raise concerns about the parameter estimates from the authors' regression model. Specifically, if the IVs are only weakly correlated with the endogenous regressors, parameter estimates may be biased, estimates may be inconsistent, tests of significance may have incorrect size, and confidence intervals may be wrong.[4–6]

The following *potential* recommendation was put to a vote of the Working Group:

***2.2: The Working Group regards the current evidence base with respect to Canadian estimates of supply-side cost-effectiveness thresholds, including the empirical research by Ochalek et al. (2018), as uncertain.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.3 Direction and magnitude of bias in the $30,000 per QALY estimate

Given the Working Group's concern with the IVs used in the Ochalek *et al.* (2018) research, members considered the potential direction and magnitude of bias in the $30,000 per QALY estimate.

At a public seminar, the chair asked the corresponding author of the Ochalek *et al.* (2018) research, Dr Karl Claxton, for his views on the implications of any weakness in the IVs.[7] Dr Claxton's response was that any weakness in the IVs would be expected to weaken the relationship between health expenditures and health outcomes, in turn resulting in an overestimate of the cost-effectiveness threshold.

The implication of Dr Claxton's remarks is that a re-estimate of the supply-side threshold with stronger IVs would be expected to be below $30,000 per QALY. However, the Working Group member who initially questioned the strength of the IVs in the Ochalek *et al.* (2018) research disagreed, arguing that the direction of bias as a result of weak IVs is unknown.

The following *potential* recommendation was put to a vote of the Working Group:

***2.3: The Working Group regards the direction and magnitude of any bias in the $30,000 per QALY estimate by Ochalek et al. (2018) to be unknown.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.4 Differences across provinces and territories

Several members noted that a different supply-side threshold would be expected for each Canadian public health care system.

Theoretically, the supply-side threshold is affected by the budget of the health care system in question, among other considerations.[8] Since each provincial and territorial health care system has its own budget, a different supply-side threshold would be expected for each.

This is consistent with the results of the work by Ochalek *et al.* (2018), which found a different supply-side threshold (in terms of cost per DALY averted) in each province and territory.[1]

The Working Group considered several potential approaches for setting a single ceiling price across all provinces and territories, including:

1. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the highest supply-side threshold;
2. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the lowest supply-side threshold;
3. A ceiling price at which the medicine is 'just' cost-effective across Canada as a whole.

A consideration of the implications of each approach is provided in the Conceptual Framework. In summary, each approach results in a different allocation of the total 'economic surplus' among 'consumers' (patients) and 'producers' (manufacturers). The first approach results in negative overall consumer surplus, the second approach results in positive overall consumer surplus, while the third approach results in zero overall consumer surplus.

Since the preferred allocation of the economic surplus is a matter for policy makers, the Working Group does not advocate for any specific approach. Instead, the Working Group recommends that any single threshold used for the purpose of informing a ceiling price be consistent with the policy intent, given the technical considerations outlined by the Working Group.

The following *potential* recommendation was put to a vote of the Working Group:

***2.4: The Working Group recognizes that each provincial and territorial public health care system has a unique supply-side cost-effectiveness threshold, and recommends that any single threshold used for the purpose of informing a ceiling price be consistent with the policy intent.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.5 Medicines with large net budget impact

In theory, adopting medicines with a large net budget impact into a budget constrained public health care system would be expected to result in a disproportionately large opportunity cost.[8,9] (Note that "net budget impact" is distinct from the "market size" consideration in section 6.)

One approach for dealing with this is to use a progressively lower supply-side threshold for medicines with progressively larger net budget impact. One member cited the empirical work by James Lomas, which estimated how the supply-side threshold for the English NHS would fall as the net budget impact of a new health technology increases.[9] For new hepatitis C treatments, which had an estimated net budget impact of £772m in the first year of use, Lomas found that the supply-side threshold would need to be adjusted down from £12,936 per QALY (the supply-side threshold for marginal changes in health care expenditure) to £12,452 per QALY.[9,10]

The Working Group was unaware of any other attempts internationally to estimate supply-side thresholds associated with non-marginal changes in health expenditures. Since no equivalent empirical estimates are available for Canada, there is no data to inform such a downwards adjustment to the Canadian supply-side threshold at the present time.

The following *potential* recommendation was put to a vote of the Working Group:

***2.5: The Working Group recognizes that, in principle, a downwards adjustment should be applied to the supply-side cost-effectiveness threshold for medicines with substantial net budget impact, but notes that there is no Canadian empirical evidence to inform the magnitude of such an adjustment at the present time.***

Members voted **10 in favour** and **2 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.6 Equity weights

The Terms of Reference tasked the Working Group with considering *"Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc)"*.

The Working Group noted that, under CADTH's 'reference case' requirements, all QALYs are assigned equal value. A justification of this position is provided in CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada' (4th Edition; pp.59-60).[11] CADTH's

reference case therefore reflects an equity position under which a 'weight' of 1 is applied to all QALYs, regardless of any characteristics of the patients, disease or technology in question.

Critically, a weight of 1 on all QALYs does not permit a ceiling price *"above opportunity cost"* for *"certain types of medicines"* but not others. The Working Group therefore considered the potential for applying different weights to some QALYs, and hence departing from CADTH's reference case assumption that all QALYs have equal value.

There is a small but growing empirical literature on the types of characteristics for which society may assign greater or lesser weight when valuing health gains.[12–18] One member provided the Working Group with a brief summary of this literature. Characteristics that are often found to be important in empirical studies include severity of illness (particularly the presence or otherwise of life threatening or progressively chronically debilitating illness), the availability of active treatment alternatives, the prevalence of disease, the type of health gain (such as a reduction in pain), and the magnitude of health gain. These factors are often found to interact with one another, and so should not be considered independently. In the opinion of this member, greater empirical work is needed to fully understand these interactions and the 'weights' that would be put on each characteristic.

Members also discussed theoretical issues associated with applying weights to some QALYs but not others. One member expressed concern that some important conceptual problems have not yet been addressed in the literature - for example, would a greater weight on QALYs for 'cancer' apply to all QALYs gained by a patient with cancer (including those gained through treatment for other diseases) or only the QALYs gained through cancer treatment (such that other QALY gains for the same patient for other diseases would be assigned different weight). There is also an ongoing and unresolved debate regarding whether weights should be applied directly to QALYs or to the cost-effectiveness threshold. The latter approach has been used by NICE in the UK but has received criticism for resulting in 'inconsistencies' in its consideration of social value.[19]

As a result of these limitations in the empirical and theoretical literature, the predominant view of members was that equity weights other than 1 should not be implemented at the present time.

There was some discussion by the Working Group regarding the potential implications of this recommendation for medicines for rare diseases. As noted in the Conceptual Framework, medicines with small market size may be expected to have a higher supply curve (at the respective quantity) than medicines with large market size. Such medicines may therefore be less profitable at a given ceiling price compared to medicines with larger market size. This issue is considered further in section 6.

The following *potential* recommendation was put to a vote of the Working Group:

***2.6: The Working Group does not recommend the implementation of 'equity weights' other than 1, as would be required to allow price ceilings above opportunity cost for some medicines but not others, due to limitations in the existing theoretical and empirical evidence base.***

Members voted **9 in favour** and **3 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.7 Clear specification of the supply-side threshold

In common with the request that any thresholds used for classifying 'Category 1' medicines be clearly specified (section 1.3.7), the two industry members emphasized the desirability that any supply-side threshold used for the purposes of informing a price ceiling be clearly specified.

As noted in the Conceptual Framework, the supply-side threshold is a key determinant of the location of the 'demand curve' for a new medicine. A technical justification for requesting that the supply-side threshold be clearly specified is that it reduces uncertainty for manufacturers regarding the location of this demand curve, and hence the producer surplus if the ceiling price is informed by this demand curve.

There was general agreement among the Working Group about the desirability of specifying the supply-side threshold, and hence providing greater clarity to manufacturers and other stakeholders regarding the location of the demand curve.

Nevertheless, as noted in the Conceptual Framework, there is also considerable uncertainty about the location of the manufacturer's 'supply curve'. This increases uncertainty regarding the set of possible ceiling prices at which consumer and producer surplus are both positive, potentially resulting in a loss of economic surplus for both consumers and producers. To minimize this uncertainty, efforts should be made to better understand the location of the supply curve for new medicines. This would complement efforts to provide greater certainty regarding the location of the demand curve through a clear specification of the supply-side threshold.

The following *potential* recommendation was put to a vote of the Working Group:

***2.7: The Working Group recommends that any estimate of the supply-side threshold adopted by the PMPRB for the purposes of informing a price ceiling be clearly specified, so as to reduce uncertainty for stakeholders.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.8 Further empirical research

Given the uncertainties in the existing empirical evidence base regarding Canadian supply-side cost-effectiveness thresholds (sections 2.3.2 and 2.3.3), there was broad support among members of the Working Group for conducting further empirical research.

Since differences in supply-side thresholds across provinces and territories are predicted by theoretical work and were observed by Ochalek *et al.* (2018) (section 2.3.4), there was also agreement that any future Canadian empirical studies should consider potential variation in estimates of supply-side cost-effectiveness thresholds across jurisdictions within Canada.

The following *potential* recommendation was put to a vote of the Working Group:

***2.8: The Working Group recommends that the PMPRB support further empirical research to estimate a supply-side cost-effectiveness threshold for Canada. This research should consider and report on variation in estimates of supply-side cost-effectiveness thresholds across jurisdictions within Canada.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 2.3.9 Specifying an ‘interim’ threshold

Since the existing empirical evidence on Canadian supply-side thresholds was considered to be uncertain, and since further empirical research will take time to conduct and report, members discussed how a threshold might be specified by the PMPRB in the interim.

#### Existing Canadian policy thresholds

One potential interim approach considered by the Working Group is for the PMPRB to specify a threshold in line with existing ‘policy thresholds’ used by Canadian HTA agencies.

The Working Group observed that no Canadian HTA agencies currently specify an explicit cost per QALY policy threshold. However, one member noted that INESSS uses an informal policy threshold of $50,000 to $100,000 per QALY, with other members providing anecdotal evidence of similar policy thresholds being used informally by other HTA agencies in Canada (with higher policy thresholds used in some cases, such as for cancer).

Another member suggested that it may be useful to understand what policy threshold is informally used by the the pan-Canadian Pharmaceutical Alliance (pCPA) in its negotiations.

One member cited a 2016 article in the Hamilton Spectator, which reported that *“the pan-Canadian Oncology Drug Review has set an unofficial threshold of $100,000 per quality-adjusted life year for new cancer medications”*, and also a 2009 letter by the Deputy Minister of Health and Long-Term Care for Ontario, which noted that the Committee to Evaluate Drugs *“typically considers a range of $40-60,000 [per] QALY as an acceptable range”*.[20,21]

Taken together, this evidence suggests that informal policy thresholds used by HTA agencies in Canada are in the region of $50,000 to $100,000 per QALY, with oncology medicines assessed at the higher end of this range and other medicines assessed relatively lower within this range.

It should be noted that none of these policy thresholds is based on an empirical assessment of the opportunity cost of adopting new medicines within Canada’s public health care systems, as would be required to specify a ‘supply-side’ threshold.

### Supply-side thresholds from other jurisdictions

Another potential interim approach is to consider empirical estimates of supply-side thresholds for other jurisdictions with similar wealth and medicine market characteristics as Canada.

The IHE report summarized three existing published estimates of supply-side thresholds for other jurisdictions:[2]

1. The work by Claxton *et al.* (2015), which estimated a supply-side threshold of £12,936 per QALY for the public health care system in the UK.[10]
2. The work by Vallejo-Torres *et al.* (2017), which estimated a supply-side threshold of between €21,000 and €25,000 per QALY for the public health care system in Spain.[22]
3. The work by Edney *et al.* (2017), which estimated a supply-side threshold of AU$28,033 per QALY for the public health care system in Australia.[23]

The chair noted that the $30,000 per QALY estimate from Ochalek *et al.* (2018) is broadly in line with these estimates, and that all three of these countries are on the proposed PMPRB12 list of countries with *"reasonably comparable economic wealth"* and *"similar medicine market size characteristics"* as Canada. Absent reasons why Canada would be considered an 'outlier' among PMPRB12 countries, one might therefore reasonably expect a future Canadian estimate of a supply-side threshold to be similar to the estimates reported in these countries. Nevertheless, given the various determinants of the supply-side threshold, some variation in estimates across countries would be expected.[8]

The following *potential* recommendation was put to a vote of the Working Group:

***2.9: The Working Group recommends that any 'interim' threshold specified by the PMPRB prior to completion of further Canadian empirical work should be informed by a comprehensive consideration of existing thresholds used by Canadian HTA agencies and empirical estimates of supply-side thresholds from other relevant jurisdictions.***

Members voted **10 in favour** and **2 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

# 3: Multiple indications

## 3.1 Terms of Reference

Within this area of focus, the Terms of Reference required the Working Group to examine and make recommendations with respect to the following considerations and questions:

> *Options for addressing medicines with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).*

## 3.2 Policy Intent

The Regulatory Impact Analysis Statement includes the following statements which provide context regarding the policy intent with respect to this area of focus:

> *"The **price paid** for a medicine should take into consideration the **value it produces**."*
>
> *(p.8, **emphasis added**)*

The PMPRB Guidelines Scoping Paper includes the following statement which provides context regarding the policy intent with respect to this area of focus:

> *"The fifth and final part of the new framework would involve the **periodic "re-benching" of drugs** to ensure that previous determinations of potential excessive pricing and/or price ceilings remain relevant in light of **new indications** (resulting in a change of market size) or changes in market conditions. Depending on the nature of the change, **the re-benching process could result in a decrease or increase in ceiling price**."*
>
> *(p.7, **emphasis added**)*

## 3.3 Summary of Deliberations

Two broad approaches were considered by the Working Group: a separate ceiling price for each indication ('indication-specific pricing'), or a single ceiling price across all indications.

There was general agreement that indication-specific pricing is the more appealing approach in principle. As noted in the Conceptual Framework, the incremental effectiveness of any medicine generally differs across indications. Indication-specific pricing would permit the ceiling price of the medicine to reflect this differing value for each indication. This would appear to closely align with the policy intent, as stated in the Regulatory Impact Analysis Statement, that "*the price paid for a medicine should take into consideration the value it produces"*.

However, although one member was of the view that multi-indication pricing may be feasible for some 'Category 1' medicines, several members expressed concern that indication-specific pricing is not possible in Canada, given current limitations in data capture and reporting.

It was noted that indication-specific pricing requires an IT infrastructure for collecting data on volume per indication. An informal review conducted by one member identified a number of different approaches internationally.[24,25] France, Germany and Australia all use indication-specific pricing, based on expected patient volumes for each indication. Italy engages in risk-sharing arrangements using indication-specific patient registries. Express Scripts in the United States is using indication-specific pricing for cancer medicines, and the UK piloted the feasibility of this approach using the Systemic Anti-Cancer Therapy Dataset (SACT) data set. Belgium and Spain have also used indication-specific pricing for expensive medicines and hospital-based medicines, respectively.

Since logistical and implementation issues were out of the scope of the Terms of Reference, Working Group members did not give detailed consideration to the feasibility of implementing indication-specific pricing in Canada. Instead, the Working Group's deliberations focused exclusively on options for specifying a single ceiling price across multiple indications.

### 3.3.1 Specifying a single ceiling price across all indications

The Working Group considered several potential approaches for setting a single ceiling price across multiple indications, including:

1. A ceiling price at which the medicine is ‘just’ cost-effective in the most cost-effective indication;
2. A ceiling price at which the medicine is ‘just’ cost-effective in the least cost-effective indication;
3. A ceiling price at which the medicine is ‘just’ cost-effective across all indications;
4. A ceiling price at which the medicine is ‘just’ cost-effective in the first indication considered by the PMPRB.

A consideration of the implications of each approach is provided in the Conceptual Framework.

In common with the different potential approaches for setting a ceiling price across provinces and territories (section 2.3.4), each approach results in a different allocation of the total economic surplus among consumers and producers. The first approach results in negative overall consumer surplus, the second approach results in positive overall consumer surplus, the third approach results in zero overall consumer surplus, while the fourth approach results in zero expected consumer surplus if manufacturers do not behave strategically when launching medicines or negative expected consumer surplus if manufacturers do behave strategically.

At the final in-person meeting, the PMPRB asked the chair to consider a fifth potential approach for setting a single ceiling price across multiple indications:

5. A ceiling price at which the medicine is ‘just’ cost-effective in one specific ‘key’ indication identified by the PMPRB.

This approach has similarities to the fourth approach considered above, insofar as the ceiling price would be based upon the cost-effectiveness of the new medicine in one indication only. It would also share an advantage that the fourth approach has over the first three approaches, insofar as the ceiling price would not need to be rebenched over time as new indications are launched (unless the ‘key’ indication were to change).

The implications for the allocation of the total economic surplus with this fifth approach depend upon whether the ‘key’ indication is more or less cost-effective than other indications. If this ‘key’ indication is the most cost-effective, then the implications are the same as for the first approach, with negative overall consumer surplus. Alternatively, if the ‘key’ indication is the least cost-effective, then the implications are the same as for the second approach, with positive overall consumer surplus. In both cases consumer surplus in the ‘key’ indication is zero.

As with the consideration of different potential approaches for setting a ceiling prices across provinces and territories (section 2.3.4), the Working Group does not advocate for any specific approach since the preferred allocation of the economic surplus is a matter for policy makers. Instead, the Working Group recommends that any single threshold used for the purpose of informing a ceiling price be consistent with the policy intent, given the technical considerations outlined by the Working Group.

The following *potential* recommendation was put to a vote of the Working Group:

***3.1: The Working Group recommends that the PMPRB specify a single ceiling price for each medicine that applies across all indications and is consistent with the policy intent.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

# 4: Accounting for uncertainty

## 4.1 Terms of Reference

Within this area of focus, the Terms of Reference required the Working Group to examine and make recommendations with respect to the following considerations and questions:

> *Options for using the CADTH and/or INESSS reference case analyses to set a ceiling price.*

> *Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.*

## 4.2 Policy Intent

The Regulatory Impact Analysis Statement includes the following statements which provide context regarding the policy intent with respect to this area of focus:

> *"In recognition of the significant expertise that can be necessary to prepare and validate cost-utility analyses,* ***reporting would be limited to those that have been prepared by a publicly funded Canadian organization, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or the Institut national d'excellence en santé et services sociaux (INESSS)****. These organizations have dedicated expertise, and they generally conduct pharmacoeconomic analyses for medicines seeking to be reimbursed by public insurers.* ***The PMPRB would consider these analyses in its evaluation of price excessiveness. It would not duplicate the work conducted by CADTH and INESSS as part of reimbursement processes****."*
>
> (pp.10-11, **emphasis added**)

None of the documents provided to the Working Group by the PMPRB included any statement regarding the policy intent with respect to *"options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling"*.

## 4.3 Summary of Deliberations

### 4.3.1 Using the CADTH and/or INESSS reference case analyses

The Terms of Reference tasked the Working Group with considering *"options for using the CADTH and/or INESSS reference case analyses to set a ceiling price"*.

Members discussed how the results of pharmacoeconomic analyses of a medicine reported by CADTH, INESSS and other Canadian HTA agencies generally differ from those reported by the manufacturer and also from each other. The industry members argued that cost-utility estimates by CADTH and INESSS *"often exhibit differences in their estimates pertaining to heterogeneous assumptions and expert opinions"*, and that this variability is *"a function of the analyst that produces the assessment and the peer reviewers that challenge the analyses"*.

Members also discussed whether the assumptions adopted by CADTH and INESSS in their 'reference case' analyses are appropriate for use by the PMPRB when setting ceiling prices. Some members suggested that the PMPRB might wish to establish its own 'reference case', clearly specifying the requirements and any necessary assumptions for pharmacoeconomic analyses used to inform ceiling prices. Although the policy intent is to *"not duplicate the work conducted by CADTH and INESSS"*, possible departures from existing CADTH and INESSS reference case assumptions include a clear specification of a supply-side cost-effectiveness threshold and a potential departure from the assumption of risk-neutrality (see section 4.3.3).

Since matters of process were beyond the remit given by the Terms of Reference, the Working Group did not consider what specific processes might be established by the PMPRB to arrive at a single set of pharmacoeconomic results from which to inform a ceiling price. Nevertheless, there was a widespread view among Working Group members that clarity is required in whatever processes are established by the PMPRB.

The following *potential* recommendation was put to a vote of the Working Group:

***4.1: The Working Group recognizes that there is variation in the results of pharmacoeconomic analyses reported by CADTH and INESSS, and recommends that the PMPRB establish clear processes for identifying how these analyses will be used to inform a ceiling price.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 4.3.1 Ensuring unbiased estimates

The Working Group noted that the most recent edition of CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada' (4th Edition) includes specific recommendations for addressing uncertainty in pharmacoeconomic analysis.[11] These include an assessment of parameter uncertainty (through probabilistic analysis), structural uncertainty (through scenario analysis), and methodological uncertainty (through a comparison of 'reference case' and 'non-reference case' analyses). INESSS has similar requirements for considering uncertainty.[26]

Some members expressed concern that not all pharmacoeconomic analyses currently satisfy these recent CADTH guidelines, and that better enforcement of these guidelines is needed to ensure that uncertainty is appropriately addressed in all pharmacoeconomic analyses considered by the PMPRB when informing ceiling prices.

Members also noted that current HTA processes at CADTH and INESSS are undertaken for the purpose of assisting public payers in making decisions related to funding and informing pricing negotiations, rather than to inform ceiling prices set by the PMPRB. There was broad agreement that the PMPRB should engage with CADTH and INESSS, and any other relevant stakeholders, regarding modifications that may be required to these processes given the proposed change in the context of their use.

While considerations of the specific processes adopted by CADTH and INESSS are beyond the scope of the Working Group, the key *technical* principle is that all pharmacoeconomic analyses should satisfy the same basic set of requirements, including a comprehensive and unbiased assessment of parameter uncertainty, structural uncertainty and methodological uncertainty.

The following *potential* recommendation was put to a vote of the Working Group:

***4.2: The Working Group recommends that all pharmacoeconomic analyses used for the purpose of informing a ceiling price should satisfy the requirements of the most recent edition of CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada', including an unbiased assessment of parameter uncertainty, structural uncertainty and methodological uncertainty.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 4.3.2 Addressing uncertainty in the point estimate

The Terms of Reference also required the Working Group to consider *"options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling"*.

It was agreed that there are a number of sources of uncertainty in any pharmacoeconomic analysis. One member noted that clinical uncertainty is typically the primary source of uncertainty when CADTH considers new medicines, particularly for rare conditions. There are also uncertainties in the incremental costs associated with new medicines.

Furthermore, since the supply-side threshold requires empirical estimation, it will inevitably be uncertain. For example, the UK research which estimated a supply-side threshold reported a probability distribution in addition to a point estimate.[10]

As noted in the Conceptual Framework, any uncertainty in the incremental costs and benefits results in uncertainty in the ICER. The price at which the ICER is equal to the supply-side threshold is also uncertain, resulting in uncertainty in the true location of the demand curve. This, in turn, results in uncertainty in the ceiling price that is consistent with the policy objective regarding the allocation of the economic surplus between consumers and producers.

Some members noted that CADTH does not always report a point estimate for the ICER, but that a point estimate would be required for the purposes of informing a ceiling price.

Members discussed how a ceiling price might be informed when there is uncertainty around the ICER. The standard approach for considering uncertainty in economic evaluations is to use the expected values of the incremental costs and incremental benefits in order to calculate an ICER. This is the approach adopted in CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada' (4th Edition).[11] This approach implicitly assumes 'risk neutrality', which is typically justified on the basis of the Arrow-Lind principle.[27]

Members also debated using the upper bound of the credible interval around the ICER. Concern was raised that this approach would provide a disincentive for manufacturers to conduct research that reduces uncertainty around the ICER, since additional uncertainty would be rewarded with a higher ceiling price. It would also result in negative expected consumer surplus.

As noted in the Conceptual Framework, if the standard approach is adopted and a ceiling price is specified at which the ICER (calculated by dividing the expected incremental costs by the expected incremental QALYs) equals the expected value of the supply-side cost-effectiveness threshold, then the expected consumer surplus would be zero. (Note that the *actual* consumer surplus may be positive or negative, but the *expected* consumer surplus would be zero).

If the policy intent is to ensure that expected consumer surplus is non-negative, and if a risk-neutral position is adopted, then this would be the highest ceiling price consistent with this policy objective. Alternatively, if a risk-adverse position is adopted, then a higher or lower ceiling price is required to mitigate this risk. Raising the ceiling price may reduce the risk that a medicine is not launched, while lowering the ceiling price may reduce the risk that a medicine results in negative consumer surplus.

Since the PMPRB's risk attitude is not known, the Working Group cannot specify the most appropriate option for informing a ceiling price. Instead, the Working Group recommends that the PMPRB adopt an approach for considering uncertainty that is consistent with its risk attitude. If the PMPRB is 'risk-neutral', this requires that the ceiling price be informed by the expected values of the incremental costs and QALYs for the medicine and the expected value of the supply-side cost-effectiveness threshold. If the PMPRB is not 'risk-neutral', then consideration should be given to setting a ceiling price that is higher or lower than that under risk neutrality, given the policy intent.

The following *potential* recommendation was put to a vote of the Working Group:

***4.3: The Working Group recommends that the PMPRB adopt an approach for considering uncertainty that is consistent with its risk attitude. If the PMPRB is 'risk-neutral', this requires that the ceiling price be informed by the expected values of the incremental costs and QALYs for the medicine and the expected value of the supply-side cost-effectiveness threshold. If the PMPRB is not 'risk-neutral', then consideration should be given to setting a ceiling price that is higher or lower than that under risk neutrality, given the policy intent.***

Members voted **10 in favour** and **2 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 4.3.3 Value of information analysis

In conventional pharmacoeconomics, the expected loss in consumer surplus that results from uncertainty is estimated using 'value of information' (VOI) analysis.

Since the focus of conventional pharmacoeconomic analysis is making a yes/no decision regarding adoption of a new medicine, conventional VOI analysis considers the expected loss associated with making the 'wrong' decision (e.g. approving a medicine that would otherwise have been rejected, or *vice versa*).

In the context of the PMPRB using 'pharmacoeconomic value' as a factor when considering the ceiling price for a new medicine, the expected loss as a result of uncertainty comes not from making the 'wrong' yes/no decision, but from setting the 'wrong' ceiling price. One member of the Working Group (Dr Christopher McCabe) circulated a technical note (Appendix 2.2) and gave a presentation (Appendix 2.4) outlining how uncertainty can be considered in this context. The Conceptual Framework built upon a number of the ideas outlined by Dr McCabe.

As noted in the Conceptual Framework, in many cases the expected impact upon consumer surplus of setting the 'wrong' ceiling price as a result of uncertainty is zero. This is the case if the medicine is still launched at a ceiling price coinciding with the *expected* demand curve, or if the medicine would *not* have launched even at a ceiling price coinciding with the *actual* demand curve. However, in cases where the medicine *would* have launched at a ceiling price coinciding with the *actual* demand curve, but does *not* launch at a ceiling price coinciding with the *expected* demand curve, uncertainty results in an expected loss in economic surplus.

In principle, the PMPRB could use VOI analysis to estimate this expected loss in economic surplus, and hence the value associated with obtaining additional sample information for one or more uncertain parameters. The results of these analyses could then be used to apply a reduction to a medicine's ceiling price to reflect the diminished expected pharmacoeconomic value as a result of uncertainty.

Conducting such VOI analyses would require an understanding of the location of the supply curve, since this is required to estimate the expected loss in economic surplus. As noted in the Conceptual Framework, in practice the location of the supply curve is unknown. Although the supply curve could be modelled with a probability distribution in order to permit VOI analysis to take place, methods for estimating the parameters of such a distribution are undeveloped.

As a result of these unresolved challenges, the Working Group does not make a recommendation on whether to use VOI analysis at the present time.

# 5: Perspectives

## 5.1 Terms of Reference

Within this area of focus, the Terms of Reference required the Working Group to examine and make recommendations with respect to the following considerations and questions:

*Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a 'significant' difference between price ceilings under each perspective.*

*How to define a 'significant' difference in price ceilings between each perspective.*

## 5.2 Policy Intent

Two months into the Working Group's deliberations, the PMPRB informed the Working Group that a **public health care system** perspective *"needs to be used to meet the policy objective of the [Regulatory Impact Analysis Statement]"*.

## 5.3 Summary of Deliberations

### 5.3.1 Acknowledgement of policy intent

Two months into the Working Group's deliberations, the PMPRB informed the Working Group that it had come to the view that a public health care system perspective *"needs to be used to meet the policy objective of the [Regulatory Impact Analysis Statement]"*.

The PMPRB noted that, in coming to this view, it had benefited from the Working Group's discussions with respect to this area of focus.

**Given this intervention from the PMPRB, the Working Group did not vote on any potential recommendations for this area of focus. Instead, the Working Group acknowledges that the policy intent is to adopt the perspective of Canada's public health care systems.**

### 5.3.2 Considerations on the choice of perspective

Prior to the PMPRB's intervention to clarify the policy intent, the Working Group discussed some of the differences between a 'public health care system' perspective and a 'societal' perspective and some of the possible implications of these differences when setting ceiling prices.

#### Differences between perspectives

As noted in CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada' (4th Edition, pp.29-31), there are differences between the costs and outcomes considered under a 'public health care system' and those considered under a 'societal' perspective.[11]

A 'public health care system' perspective only considers costs borne by the public health care payer, and the only outcomes considered are health effects relevant to patients and caregivers.

A 'societal' perspective also considers costs that fall on private insurers (e.g. medicines that are not covered by the public payer), other government sectors (e.g. social services and affordable housing), and patients or caregivers (e.g. out-of-pocket payments and travel costs). In addition, a societal perspective considers productivity costs (e.g. due to reduced working capacity or absence from work) and broadens the consideration of outcomes to include non-health effects relevant to patients and caregivers (e.g. better educational achievements).

#### Private insurers and out-of-pocket payers

Industry members on the Working Group expressed concern that, under a health care system perspective, costs borne by private insurers and out-of-pocket payers would not be taken into account. These members also argued that the willingness-to-pay of some private payers is higher than that of public payers, which would not be taken into account through consideration

of a supply-side cost-effectiveness threshold. It was further argued that savings to private payers through a lower ceiling price may not be passed on to individuals or employers.

In support of this position, some members noted that the willingness-to-pay of private payers may be better reflected by estimates of a 'demand-side' cost-effectiveness threshold rather than a supply-side threshold. As outlined in the IHE report, there are reasons to expect that a demand-side cost-effectiveness threshold would be higher than a supply-side threshold.

In response, one member argued that it is not meaningful to consider the willingness-to-pay of private payers in isolation from the willingness-to-pay of public payers, on the basis that the market for private payers could not exist in its present state without a sustainable public health care system. According to this member, it is therefore reasonable for the PMPRB to set a ceiling price that ensures the sustainability of the public health care system, even if this is lower than a ceiling price based on the willingness-to-pay of private payers.

One member supported a societal perspective on the basis that the PMPRB should account for *"the many rare disease patients who rely on alternatives to the public health care system"*.

### Problems with a societal perspective

A number of members discussed problems with the consideration of a societal perspective.

One member suggested that adopting a societal perspective, rather than a public health care system perspective, results in *"increased uncertainty with no real impact"*. Another member argued that adopting a societal perspective implies that policy makers are willing to trade health benefits for other societal benefits, which may not be the case.

Several members expressed concern with the consideration of productivity costs that would be made under a societal perspective. Some cited the technical difficulty of estimating productivity costs and the additional uncertainty that results. Other pointed out ethical concerns, including the potential for productivity to be valued less for those with lower earning power, including women and the retired, which may be considered discriminatory.

# 6: Market size factor

## 6.1 Terms of Reference

Within this area of focus, the Terms of Reference required the Working Group to examine and make recommendations with respect to the following considerations and questions:

> *Approaches to derive an appropriate affordability adjustment to a medicine's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' approach).*

## 6.2 Policy Intent

The Regulatory Impact Analysis Statement includes the following statements which provide context regarding the policy intent with respect to this area of focus:

> *"The addition of this [**market size**] factor in the Regulations could enable the PMPRB to develop **market impact tests** for medicines that are likely to pose **affordability challenges** for insurers due to the **market size** for the medicine. The **impact of an excessive price** is a function of both **price** and **volume**; the **larger the size of the market** for the medicine in Canada, the **greater the impact of its price**".*
>
> *(p.8, **emphasis added**)*

> *"The introduction of **GDP in Canada** and **GDP per capita in Canada** as a price regulatory factor would provide the PMPRB with measures of **ability to pay for medicines at the national and individual level**. The inclusion of this factor would allow the PMPRB to assess the **impact of a medicine's price on the finances of consumers and insurers**. It could also enable the PMPRB to develop **market impact tests** for medicines that are likely to pose **affordability challenges** for insurers due to the **market size** for the medicine."*
>
> *(p.9, **emphasis added**)*

The Proposed Regulatory Text includes the following text:

> *"4.4 For the purposes of paragraph 85(1)(e) of the Act, the other factors that the Board must take into consideration to determine whether a medicine that is sold in any market in Canada after December 31, 2018 is being or has been sold at an excessive price are the following:*
>
> *A. the **pharmacoeconomic value** in Canada of the medicine and that of other medicines in the same therapeutic class;*
> *B. the **size of the market** for the medicine in Canada and in countries other than Canada; and*
> *C. the **gross domestic product in Canada** and the **gross domestic product per capita in Canada**."*
>
> *(p.24, **emphasis added**)*

The PMPRB Guidelines Scoping Paper includes the following statement which provides context regarding the policy intent with respect to this area of focus:

> *"The second part of the test would assess whether a drug that meets the cost effectiveness threshold should have its **price further adjusted** because of its **expected impact on payers within the first three to five years from launch** (assuming appropriate clinical utilization and no rationing of care). This test would consider the **anticipated market size of the new drug against GDP growth**, with the latter serving as a rough proxy for **how much Canadian consumers can afford to pay for the new patented drugs that come to market on an annual basis**. The test could also be used to allow a **price adjustment upward** in instances where a drug has a **very high opportunity cost but very small market impact due to the extreme rarity of the condition it is indicated to treat**."*
>
> *(p.6, **emphasis added**)*

> *"The fifth and final part of the new framework would involve the **periodic "re-benching"** of drugs to ensure that previous determinations of potential excessive pricing and/or price ceilings remain relevant in light of **new indications (resulting in a change of market size)** or **changes in market conditions**. Depending on the nature of the change, the re-benching process could result in a **decrease or increase in ceiling price**."*
>
> *(p.7, **emphasis added**)*

The PMPRB Framework Modernization Presentation includes the following statements which provide context regarding the policy intent with respect to this area of focus:

> *"Drugs that are expected to have a **significant market size and impact on the healthcare system** will have a **lower ceiling price** to deter rationing."*
>
> *(p.7, **emphasis added**)*

The PMPRB Framework Modernization Presentation includes the following slides which provide context regarding the policy intent with respect to this area of focus:

## Part III: MRP for Category 1 drugs (continued)

- Step 2: application of market size and GDP factors
  - A Category 1 drug that meets the applicable $/QALY ceiling may still face an adjustment in price if the application of the market size and GDP factors raise affordability concerns.
  - Using new drug contribution to GDP and GDP growth over the last five years, the PMPRB is estimating a threshold of $XM per new drug.
  - New Category 1 drugs with an estimated market size that exceeds this threshold within any of its first five years of sale will require further price adjustments.
  - The adjustment would see the MRP reduced by a certain percentage discount which would increase as the expected market size increases (see next slide).
  - The market size threshold would also increase annually based on GDP growth and/or CPI.

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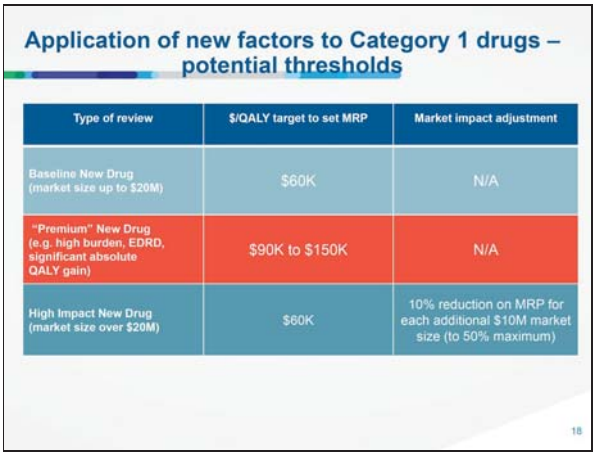

## Application of new factors to Category 1 drugs – potential thresholds

| Type of review | $/QALY target to set MRP | Market impact adjustment |
|---|---|---|
| Baseline New Drug (market size up to $20M) | $60K | N/A |
| "Premium" New Drug (e.g. high burden, EDRD, significant absolute QALY gain) | $90K to $150K | N/A |
| High Impact New Drug (market size over $20M) | $60K | 10% reduction on MRP for each additional $10M market size (to 50% maximum) |

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## 6.3 Summary of Deliberations

The Working Group noted that the *Proposed Regulatory Text* includes separate consideration of the pharmacoeconomic value, market size, and GDP factors. The 'affordability adjustment' that the Working Group was tasked with considering would therefore be applied separately from the consideration of 'pharmacoeconomic value'.

### 6.3.1 Implications for consumer and producer surplus

The proposed market size adjustment includes a potential upwards ceiling price adjustment for medicines with small market size and, independently, a potential downwards ceiling price adjustment for medicines with large market size.

As shown in the Conceptual Framework, the first of these adjustments would have the effect of increasing the producer surplus, at the expense of consumer surplus, for medicines with small market size. The second of these adjustments would increase the consumer surplus, at the expense of producer surplus, for medicines with large market size.

An additional implication of the first adjustment is that, by increasing the profitability of medicines with small market size, this might result in greater access to such medicines. The potential for this is demonstrated in Figure 13B of the Conceptual Framework. This adjustment may therefore provide a means for mitigating the concerns expressed by one member regarding the potential impact of a lower ceiling price on access to orphan drugs (see section 2.3.7).

Since the desired allocation of the economic surplus among consumers and producers is a matter for policy makers, the Working Group does not take a position on the appropriate magnitude of any proposed market size adjustments. Instead, the Working Group recommends that the PMPRB consider the implications of any proposed market size adjustments for the allocation of the economic surplus, and ensure that these are consistent with the policy intent.

The following *potential* recommendation was put to a vote of the Working Group:

***6.1: The Working Group recommends that the PMPRB consider the implications of any market size adjustments for the allocation of consumer and producer surplus, and ensure that these are consistent with the policy intent.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 6.3.2 Potential incentives and disincentives

The Working Group discussed several potential incentives and disincentives associated with implementation of a market size adjustment.

It was noted that the estimated market size of a medicine at launch is uncertain. A market size adjustment based on a medicine's *estimated* market size might therefore result in a downwards adjustment to the ceiling price for a medicine which does not ultimately achieve a large market size. Conversely, a downwards adjustment might *not* be applied to a medicine that unexpectedly achieves a large market size. To minimize any resulting disincentives, the market size adjustment would ideally be applied to *actual* market size rather than expected market size.

If the reduction in ceiling price for medicines with large market size is large, then manufacturers may be incentivized to reduce the quantity supplied so as to avoid the reduction in the ceiling price. As demonstrated in the Conceptual Framework, this risk may be particularly acute if the medicine in question has multiple indications, and if pricing across all indications is based upon the least cost-effective indication. This is because this pricing approach may already provide an incentive for manufacturers to avoid launching in one or more indications, and the addition of a market size adjustment may exacerbate this risk.

By providing a higher ceiling price for medicines with low market size, a market size adjustment might also relatively incentivize the development of such medicines. Over time, a reduction in medicines with large market size and an increase in medicines with small market size might result in progressively smaller gains and progressively larger losses in consumer surplus.

The following *potential* recommendation was put to a vote of the Working Group:

***6.2: The Working Group recommends that the PMPRB consider the potential incentives and disincentives that might result from the application of any market size adjustments.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 6.3.3 GDP and GDP per capita

#### US 'ICER' approach

The Terms of Reference cited the Institute for Clinical and Economic Review (ICER) as providing a potential approach to inform an 'affordability adjustment'.

*(Note that the acronym 'ICER' has been used elsewhere in this report to refer to a medicine's 'incremental cost-effectiveness ratio', which is the more common usage of this acronym. Within this section only, 'ICER' will be used to refer to the Institute for Clinical and Economic Review).*

One member reached out to Dr Dan Ollendorf, former Chief Scientific Officer at ICER, who provided a copy of his submission to Health Canada during the consultation period on the proposed amendments. On behalf of ICER, Dr Ollendorf noted that *"we are supportive of the PMPRB's efforts to better align pricing of pharmaceuticals with value"*, and that *"we applaud the PMPRB for considering amendments that provide additional focus on pricing innovative medicines according to the value they bring to individual patients, families, and the overall health system"*. However, Dr Ollendorf raised a note of caution regarding the proposed 'affordability' criteria, noting *"several technical challenges with implementing the market size factor for price setting at ICER"*. Among these, *"there was a challenge in interpreting an explicit linkage of budget impact results to a price", "it proved difficult for individual decision-makers to make sense of a national budget threshold"*, and *"any explicit linkage of a threshold to price-setting required ICER to estimate what 'unmanaged' uptake would look like, which was extraordinarily difficult"*.

#### UK approach

During the Working Group's deliberations, it was announced that the UK's new five-year 'Voluntary Pricing and Access Scheme' for branded medicines, which came into force on 1 January 2019, includes a 2% cap on nominal annual growth of the total medicines bill.

#### Using GDP to update thresholds

The Working Group discussed how any thresholds specified for the criteria used to classify medicines as 'Category 1', as well as any supply-side threshold specified by the PMPRB, may need to be periodically revised in response to changes in GDP and GDP per capita over time.

It was noted that the supply-side threshold for any specific province or territory is a function of the budget for the respective health care system, in addition to a number of other factors.[8] A change in GDP or GDP per capita over time would therefore be expected to have an indirect impact upon the supply-side threshold through a change in the size of the health care budget. It follows that the supply-side threshold should not be adjusted directly to account for changes in GDP or GDP per capita; rather, it should be recalculated periodically to reflect changes in the

size of provincial and territorial health care budgets and the marginal productivity of health care services that face displacement from the adoption of new medicines.

The following *potential* recommendation was put to a vote of the Working Group:

***6.3: The Working Group recommends that the PMPRB periodically reconsider any specified thresholds in response to changes in GDP and GDP per capita over time, including the supply-side cost-effectiveness threshold and any thresholds for criteria used to classify medicines as 'Category 1'.***

Members voted **12 in favour** and **0 against** this potential recommendation.

This was therefore **adopted** as a formal recommendation of the Working Group.

### 6.3.4 Considerations beyond 'pharmacoeconomic value'

The chair noted that application of both the 'market size' and 'gross domestic product' factors require considerations beyond those made in assessments of 'pharmacoeconomic value'.

Since the Working Group was primarily composed of experts in pharmacoeconomics, there may be important technical considerations for the application of these two factors that are beyond the expertise of the Working Group.

# Appendix 1: Conceptual Framework

## A1.1 Foreword

This Conceptual Framework was drafted by the chair prior to the final meeting of the Working Group. Its purpose was to guide the Working Group in making consistent recommendations across all six areas of focus, while respecting the policy intent and the range of views expressed by members of the Working Group throughout their deliberations.

### A1.1.1 Policy intent

This framework incorporates the following components of the policy intent:

During the Working Group's deliberations, the PMPRB stated that the most appropriate perspective to adopt when considering the 'pharmacoeconomic value' factor described in Amendment 4.4(a) in the Regulations Amending the Patented Medicines Regulations is that of *Canada's publicly funded health care systems*.

The Regulatory Impact Analysis Statement (Appendix 5.1) states that the *quality-adjusted life year (QALY)*, as used in cost-utility analysis, is regarded as the "gold standard" approach to considering the economic value of new medicines.

In a July 2018 document prepared for the Working Group (Appendix 5.4), the PMPRB clarified that the purpose of the PMPRB is to ensure that patentees do not change excessive prices *during the statutory monopoly period*.

The PMPRB clarified to the Working Group that its mandate is to *protect consumers from excessive pricing*, and *not* to ensure that products are launched into the market.

### A1.1.2 Deliberations of the Working Group

This framework reflects the following considerations from the Working Group's deliberations:

The Terms of Reference required the Working Group to consider potential approaches for allowing higher ceiling prices for some medicines on the basis of specific characteristics. This would require departing from the position that all QALYs have equal value, allowing for 'equity weights' (other than 1) to be applied to some QALYs but not others. Although there is an emerging body of empirical evidence, it was agreed by the Working Group that methods to apply equity weights (other than 1) are undeveloped at the present time. For the purposes of this conceptual framework, QALYs are therefore assigned equal value.

The Working Group considered several approaches for setting a single ceiling price across provinces and territories, including:

1. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the highest $k$ (such that the ICER equals this highest $k$);
2. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the lowest $k$ (such that the ICER equals this lowest $k$);
3. A ceiling price at which the medicine is 'just' cost-effective across Canada as a whole (such that the ICER equals a 'weighted average' of $k$ across Canada).

Although the Working Group agreed that a different ceiling price should be specified for each indication *in principle*, concerns were raised about the feasibility of doing this in Canada at the present time. The Working Group therefore considered various approaches for setting a single ceiling price across multiple indications, including:

1. A ceiling price at which the medicine is 'just' cost-effective in the most cost-effective indication (such that the ICER equals $k$ in this indication);
2. A ceiling price at which the medicine is 'just' cost-effective in the least cost-effective indication;
3. A ceiling price at which the medicine is 'just' cost-effective across all indications (such that a 'weighted average' of the ICER across all indications equals $k$);
4. A ceiling price at which the medicine is 'just' cost-effective in the first indication considered by the PMPRB (such that the ICER equals $k$ in this indication).

## A1.2 Economic principles

When considering how the price of any good ought to be determined, it is informative to consider some fundamental economic principles.

At any given price, the ‘economic surplus’ from a good is the sum of two parts:

- The ‘consumer surplus’, which is the benefit obtained by consumers because they are able to purchase the good at a price lower than their ‘willingness-to-pay’;
- The ‘producer surplus’, which is the benefit obtained by producers because they are able to sell the good at a price higher than their ‘willingness-to-accept’.

### A1.2.1 Standard models

Mainstream economics has a number of standard models which describe how consumers and producers behave under different market conditions, and the implications of this for the allocation of the economic surplus between consumers and producers. Among many possible models, the following are of particular relevance for the Working Group’s deliberations:

1. In a perfectly competitive market, an equilibrium price arises at which there is positive consumer surplus and positive producer surplus. This is because most consumers pay a price lower than their maximum willingness-to-pay (as represented by a downwards sloping demand curve), while most producers receive a price higher than their minimum willingness-to-accept (as represented by an upwards sloping supply curve). The overall economic surplus is positive and allocated between consumers and producers.

2. In a monopolistic market with a single price, the single producer reduces output and raises its price so as to maximize the producer surplus. Consumer surplus is diminished but remains positive, since some consumers still pay a price below their willingness-to-pay. However, the overall economic surplus is diminished because reducing output results in a ‘deadweight loss’: some consumers are willing to pay a price above the producer’s supply curve, but the producer would prefer not to supply to those consumers since greater profits arise by supplying fewer consumers at a higher price.

3. In a monopolistic market with perfect price discrimination, the producer charges a different price to each consumer so as to extract the entire economic surplus. Consumer surplus is zero, since all consumers pay a price equivalent to their willingness-to-pay. The entire overall economic surplus is retained by the producer.

In order to consider the consumer and producer surplus that might arise from the PMPRB setting a ceiling price on a new medicine, we must first specify demand and supply curves.

### A1.2.2 Demand curve for a medicine

The demand curve reflects society's willingness-to-pay for the medicine in question.

It is for the PMPRB, rather than members of the Working Group, to define the components of this demand curve. The Working Group therefore defers to the policy intent when considering the relevant components of the demand curve.

> During the Working Group's deliberations, the PMPRB stated that the most appropriate perspective to adopt when considering the 'pharmacoeconomic value' factor described in Amendment 4.4(a) in the Regulations Amending the Patented Medicines Regulations is that of *Canada's publicly funded health care systems*.

> The Regulatory Impact Analysis Statement (Appendix 5.1) states that the *quality-adjusted life year (QALY)*, as used in cost-utility analysis, is regarded as the "gold standard" approach to considering the economic value of new medicines.

> In a July 2018 document prepared for the Working Group (Appendix 5.4), the PMPRB clarified that the purpose of the PMPRB is to ensure that patentees do not change excessive prices *during the statutory monopoly period*.

In light of this policy intent, a reasonable specification of the demand curve for a new medicine is based upon the net impact upon the lifetime health of patients associated with adopting the medicine within Canada's publicly funded health care systems for the duration of the statutory monopoly period, where health is measured in QALYs and discounted to a present value.

The net impact of a new medicine upon patient health is a function of two components:

1. The gain in health experienced by patients who receive the new medicine; and
2. The loss in health experienced by other patients whose health care subsequently receives less funding than it would have done in the absence of the new medicine.

The Terms of Reference required the Working Group to consider potential approaches for allowing higher ceiling prices for some medicines on the basis of specific characteristics. This would require departing from the position that all QALYs have equal value, allowing for 'equity weights' (other than 1) to be applied to some QALYs but not others. Although there is an emerging body of empirical evidence, it was agreed by the Working Group that methods to apply equity weights (other than 1) are undeveloped at the present time. For the purposes of this conceptual framework, QALYs are therefore assigned equal value.

The gain in health for patients who receive the medicine is routinely calculated by CADTH and INESSS as part of their existing methods for conducting economic evaluations, and is typically denoted as $\Delta H$ (where the delta refers to 'incremental' and $H$ refers to 'health benefit').

The loss in health experienced by other patients is commonly referred to as the 'opportunity cost' of funding the new medicine, although it has been argued that the true opportunity cost is greater than just this 'displaced health'.[28,29]

Since the patients who incur these health losses are typically unidentifiable, the standard approach for estimating the magnitude of this health loss is to divide the incremental costs of the new medicine, commonly denoted as $\Delta C$, by a parameter reflecting the 'shadow price' of the relevant health care budget constraint, typically denoted as $k$. This latter parameter is also commonly referred to as the 'supply-side cost-effectiveness threshold'.

For example, in the case studies provided to the Working Group by the PMPRB, it was assumed that $k$ is $60,000 per QALY (the empirical evidence for specifying $k$ is considered elsewhere in this report). This implies that every additional $60,000 in cost imposed by a new medicine upon Canada's public health care systems results in a health loss of 1 QALY.

Assuming that there is only one indication for the new medicine, and assuming a single value of $k$ that applies regardless of the quantity of medicine supplied (assumptions reconsidered later), the demand curve for the new medicine is a perfectly elastic horizontal line that plots the ceiling price at which the health gain from the medicine is exactly offset by the health loss, such that the net health benefit is zero. That is, the demand curve plots the ceiling price at which

$$\Delta H = \Delta C / k \,. \qquad (1)$$

Rearranging equation (1), it follows that the demand curve plots the ceiling price at which the incremental cost-effectiveness ratio (ICER) of the new medicine is equal to $k$:

$$\Delta C/\Delta H = k\,. \qquad (2)$$

For the hypothetical medicine in Figure 1, the ICER is equal to $k$ at a ceiling price of $P_1$, such that the demand curve is also plotted at this ceiling price.

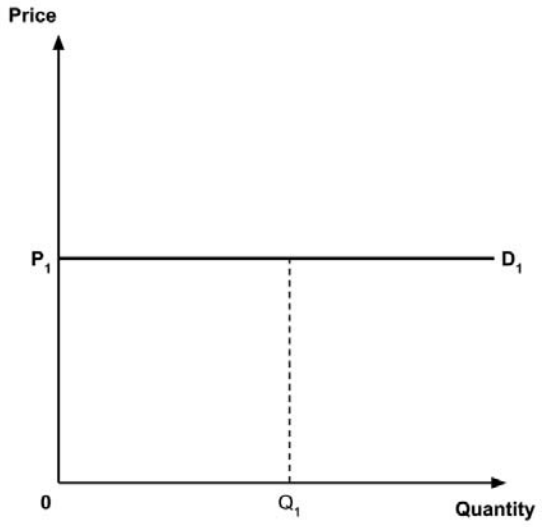


**Figure 1: Demand curve for a hypothetical medicine ($D_1$)**

The PMPRB provided the Working Group with a number of case studies (Appendix 6). For each of these case studies, the reported 'PV Threshold Price' is the ceiling price at which the medicine has an ICER of $60,000 per QALY. Since $60,000 per QALY is the PMPRB's assumed value of $k$, it follows that every additional $60,000 spent on each new medicine at the 'PV Threshold Price' would provide 1 additional QALY but is assumed to displace 1 additional QALY in other patients, such that the net health benefit is zero. It follows that the demand curve for the new medicine considered in each case study would be plotted at the 'PV Threshold Price'.

Since the ceiling price at which the ICER is equal to $k$ varies across medicines, each medicine has a different demand curve. The more cost-effective a medicine is, and hence the more QALYs produced at a given ceiling price, the higher the ceiling price at which the ICER is equal to $k$ and the higher the demand curve (Figure 2A). Conversely, the less cost-effective a medicine is, the lower the demand curve (Figure 2B).

It follows that the developers of future medicines have two mechanisms by which they can raise the demand curve for their medicine upon launch: improve the effectiveness of the medicine (and the resulting health gain) or reduce the price (and the resulting health loss).

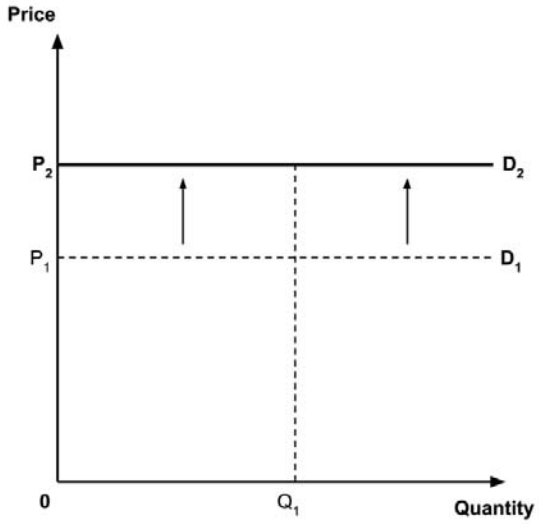


**Figure 2A: Demand curve for a more cost-effective medicine ($D_2$)**

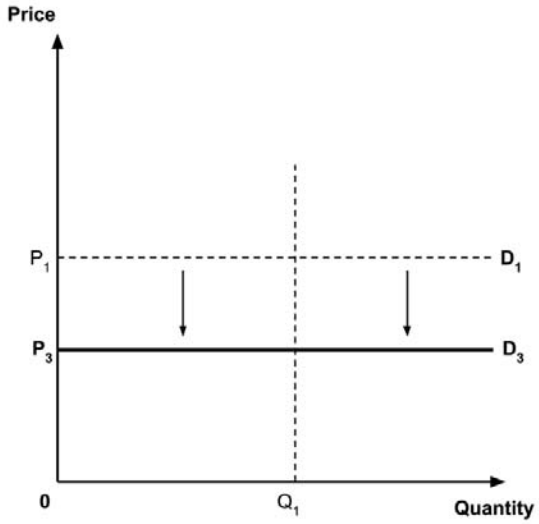


**Figure 2B: Demand curve for a less cost-effective medicine ($D_3$)**

## A1.2.3 Supply curve for a medicine

The supply curve plots the lowest price that a manufacturer would be willing to accept for a medicine. This is sometimes referred to as the ‘reservation’ (or ‘reserve’) price of the medicine.

The supply curve is a function of a number of potential considerations, including the initial costs associated with developing the medicine, the marginal costs of production, and the potential implications for pricing in other jurisdictions as a result of ‘reference pricing’.

It is important to note that the supply curve in a specific jurisdiction does not necessarily reflect only the marginal costs of production or the required return on investment for the manufacturer. Due to the possibility of reference pricing, a manufacturer might be unwilling to accept a price in a specific jurisdiction, even if this covers the marginal costs of production and provides a sufficient return on investment in that jurisdiction, if this results in a lower price in one or more other jurisdictions. One means of mitigating this possibility is through the use of confidential pricing arrangements, such that the price actually paid in a specific jurisdiction is lower than the ‘list price’ used by other jurisdictions for the purpose of reference pricing. Confidential pricing arrangements may therefore be expected to lower the supply curve, since the implications for reference pricing in other jurisdictions are no longer a relevant factor.

Regardless of whether reference pricing is a relevant factor, the components of the supply curve are complex. Furthermore, compared to the components of the demand curve (such as $k$),

relatively little empirical research has been conducted into the components of the supply curve, with existing research focused primarily on estimating the costs associated with research and development (rather than the expected reservation price). As a result of this asymmetry, the supply curve for each new medicine is highly uncertain. For the purposes of this framework, the medicine's supply curve will therefore be treated as unknown (and plotted as a dashed line).

Despite being unknown, we may reasonably expect the supply curve for a medicine to have the following basic properties:

1. A relatively high intercept on the vertical axis, reflecting the substantial initial costs associated with researching and developing the medicine;

2. A downwards slope, reflecting a declining per-patient cost of supplying the medicine as the quantity supplied increases. This declining per-patient cost arises from the ability to spread the initial costs of research and development across a greater number of patients, and also potential economies of scale in the production of the medicine.

Since initial research and development costs and production costs vary across medicines, each medicine would be expected to have a different supply curve.

For example, recent empirical work found that the initial development costs for an orphan drug (with a small patient population, resulting in a relatively small quantity supplied) are $291m USD (average capitalized clinical cost), compared to $412m USD for a non-orphan drug.[30]

Other recent work has found that the research and development costs associated with a new orphan drug are smaller than those for a non-orphan drug, but, given the smaller patient population, a higher per-patient price is required for orphan drugs to sustain a similar return on investment than non-orphan drugs.[31]

Figure 3 plots possible supply curves for two hypothetical medicines. Although both medicines are assumed to have large development costs, the first medicine (represented by supply curve $S_1$) will be supplied at a lower price, for any given quantity, than the second medicine (represented by supply curve $S_2$). For example, at a given quantity, $Q_1$, the manufacturer of the first medicine is willing to accept a price of $P_4$, whereas the manufacturer of the second medicine requires a higher price of $P_5$. Among many other possible reasons, this might be due to the first medicine having relatively lower marginal costs of production.


**Figure 3: Supply curves for two hypothetical medicines, with relatively low ($S_1$) and high ($S_2$) marginal costs of production**

## A1.2.4 Economic surplus

The demand and supply curves may be used to consider the 'economic surplus' that results from adoption of a new medicine and, at any given ceiling price, the distribution of this economic surplus between consumers (patients) and producers (the manufacturers of new medicines).

When demand and supply curves are plotted on the same figure, the economic surplus is illustrated by the area of the region below the demand curve and above the supply curve, minus any area above the demand curve but below the supply curve, and bounded between the vertical axis and the quantity of medicine adopted.

For example, Figure 4A plots the demand ($D_1$) and supply ($S_1$) curves for a medicine with a relatively low supply curve. At a quantity of $Q_1$, the economic surplus is positive and illustrated by the area of region 2 minus the area of region 1.

Figure 4B, by contrast, plots the demand ($D_1$) and supply ($S_2$) curves for a medicine with a relatively high supply curve. Since the supply curve lies entirely above the demand curve, adopting this medicine at a quantity of $Q_1$ would result in a negative economic surplus, as illustrated by the area of region 3.

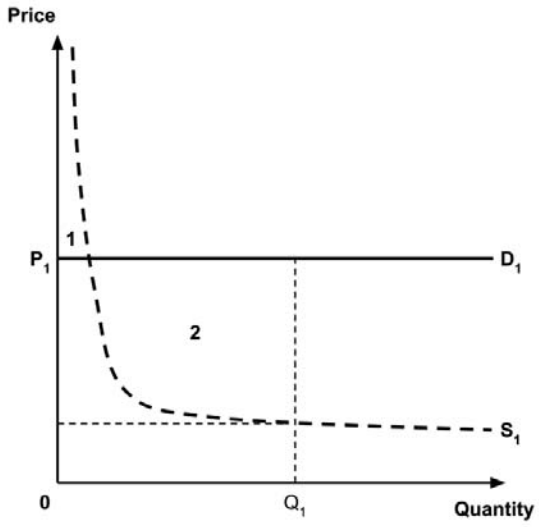


**Figure 4A: Demand and supply curves for a medicine with a relatively low supply curve, resulting in a positive total economic surplus**


**Figure 4B: Demand and supply curves for a medicine with a relatively high supply curve, resulting in a negative total economic surplus**

## A1.2.5 Defining consumer and producer surplus

Given the policy intent, the 'consumer surplus' arising from adoption of a new medicine reflects the net health benefit (in QALYs) for patients within Canada's public health care systems.

The 'producer surplus', meanwhile, reflects profits for the manufacturers of new medicines.

## A1.2.6 Allocating a positive economic surplus

How the economic surplus might be allocated among 'consumers' (patients) and 'producers' (manufacturers) depends upon whether this overall economic surplus is positive or negative.

If the economic surplus is positive, as in Figure 5A, then there is a range of possible ceiling prices at which consumer and producer surplus are both positive, such that adoption of the new medicine would provide a net benefit to patients and also the manufacturer.

The upper bound of this range is a ceiling price corresponding to the demand curve ($P_1$ in Figure 5A), at which the ICER is $k$. At this ceiling price, the entirety of the economic surplus (illustrated by the area of region 2 minus the area of region 1) is allocated to the producer, such that the consumer surplus is zero. This is analogous to the allocation of consumer and producer

surplus that would arise in a conventional model of monopoly with perfect price discrimination (in which the producer extracts the entire economic surplus).

The lower bound of this range is a ceiling price at which producer surplus is zero ($P_6$ in Figure 5B). At this ceiling price, the ICER is below $k$ and consumer surplus is positive, illustrated by the combined area of regions 4 and 5. Producer surplus is zero, illustrated by the area of region 6 minus the combined area of regions 1 and 4. Note that the overall economic surplus remains the same as in Figure 5A, and is equivalent to the combined area of regions 1, 5 and 6 only (since area 4 constitutes both a benefit for consumers and a loss for producers).

A ceiling price above $P_1$ (so the ICER exceeds $k$) would result in negative consumer surplus (such that the new medicine would diminish population health), and a ceiling price below $P_6$ would result in negative producer surplus (such that the new medicine is not profitable).

It follows that only a ceiling price between $P_1$ and $P_6$ in Figure 5B would result in both positive consumer surplus and positive producer surplus. At any ceiling price within this range, the ICER of the new medicine is lower than $k$. Compared to the allocation of consumer and producer surplus which arises when the ceiling price corresponds to the demand curve (such that the ICER is exactly $k$), this allocation is closer to that which would arise in a conventional model of a competitive market (in which consumer and producer surplus are both positive).


**Figure 5A: At a price of $P_1$, the entire economic surplus is allocated to the producer (region 2 minus region 1)**


**Figure 5B: At a price of $P_6$, the entire economic surplus is allocated to the consumer (regions 4 and 5)**

## A1.2.7 Allocating a negative economic surplus

If the economic surplus is negative, as in Figure 4B, then there are no possible ceiling prices at which both consumer and producer surplus are positive.

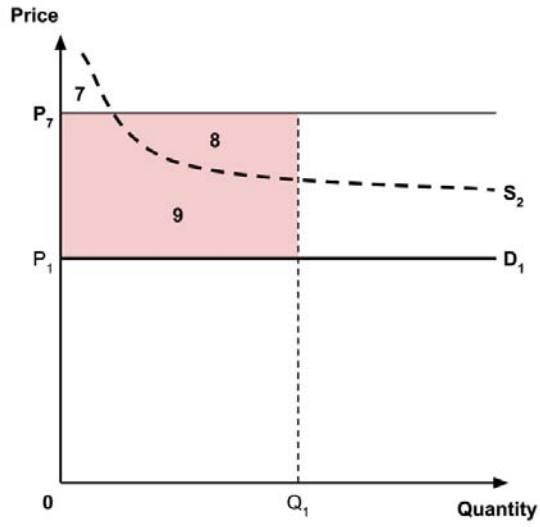


**Figure 6: Where the supply curve lies above the demand curve, producer surplus cannot be positive unless consumer surplus is negative**

Although a higher ceiling price can be sought for the medicine at which producer surplus is positive, this will result in negative consumer surplus. The consequence of a negative consumer surplus is that other patients will incur a greater loss in health than will be gained by the patients who receive the new medicine, in turn diminishing population health.

For example, in Figure 6, a ceiling price of $P_7$ results in a positive producer surplus, as illustrated by the area of region 8 minus the area of region 7. However, consumer surplus is negative, as illustrated by the combined area of regions 8 and 9. Attempts to avoid this negative consumer surplus by lowering the ceiling price will also result in negative producer surplus.

The potential for the supply curve to lie above the demand curve is a particularly important consideration for medicines that are supplied to relatively few patients, such as orphan drugs, for which the supply curve may be more likely to be higher than the demand curve at the relevant quantity.

## A1.3 Pricing across provinces and territories

The IHE report considered the various determinants of $k$.[2]

A key determinant is the size of the relevant health care budget, with larger per-capita health care budgets resulting in higher values of $k$ (all else equal).

Other determinants include the marginal productivity of existing health care activities that might experience reduced funding or displacement if a new medicine is adopted.[8]

### A1.3.1 Variations in 'k' across provinces and territories

Since provinces and territories in Canada have some autonomy in setting health care budgets and prioritizing spending, it follows that $k$ would be expected to vary by province and territory.

This is supported by the empirical work by Ochalek *et al.* (2018), which reported varying estimates of the marginal 'cost per DALY averted' across provinces and territories.[1] Using data from Claxton *et al.* (2017), this report found higher estimates in the territories (ranging from $30,633 per DALY averted in Yukon to $52,191 per DALY averted in the Northwest Territories), and lower estimates across the provinces (ranging from a low of $16,425 per DALY averted in Prince Edward Island to a high of $26,060 per DALY averted in Alberta).

Note that, although these estimates were reported in terms of marginal 'cost per DALY averted', similar variation in estimates would be expected if these were instead reported in terms of marginal 'cost per QALY gained', which is how $k$ should be specified given the policy intent.

### A1.3.2 Implications for the opportunity cost of new medicines

An important implication of this variation in $k$ is that the opportunity cost of adopting a new medicine would be expected to differ across provinces and territories. The lower $k$ is in any province or territory, the greater the expected opportunity cost associated with adopting a new medicine (in terms of health forgone by other patients).

For example, based upon the report by Ochalek *et al.* (2018), every additional $1m spent on new medicines in Prince Edward Island would have an opportunity cost of approximately 60 DALYs, but every additional $1m spent on new medicines in Alberta would have a smaller opportunity cost of approximately 40 DALYs. All else equal, the net health benefit of any new medicine would therefore be expected to be smaller in Prince Edward Island than in Alberta.

### A1.3.3 Implications for the demand curve

Since the demand curve plots the ceiling price at which the ICER of the new medicine is equal to $k$ (equation 2), it follows that the demand curve will be higher in provinces and territories with larger estimates of $k$.

For example, based on the empirical work by Ochalek *et al.* (2018), we might expect the lowest demand curve in Prince Edward Island, the highest provincial demand curve in Alberta, and the highest demand curve overall in the Northwest Territories.

The width of each demand curve (the quantity demanded) would also be expected to differ across provinces and territories, since the number of patients receiving each new medicine will vary due to differences in population size and demographics.

### A1.3.4 Approaches for setting a single ceiling price

The Working Group considered several approaches for setting a single ceiling price across provinces and territories, including:

1. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the highest $k$ (such that the ICER equals this highest $k$);
2. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the lowest $k$ (such that the ICER equals this lowest $k$);
3. A ceiling price at which the medicine is 'just' cost-effective across Canada as a whole (such that the ICER equals a 'weighted average' of $k$ across Canada).

Figures 7A to 7D demonstrate the implications of each of these approaches using a simplified model of a new medicine provided to patients across two provinces. In this model, 'Province A' has a higher $k$ than 'Province B', such that the ceiling price at which the ICER of the medicine equals $k$ in 'Province A' is $P_8$. Given its size and demographics, 'Province A' demands a quantity of medicine $Q_2$. 'Province B' demands a smaller quantity, $Q_3$ - $Q_2$, and has a lower $k$ than 'Province A', such that the ICER would equal $k$ for this province at a ceiling price of $P_9$.

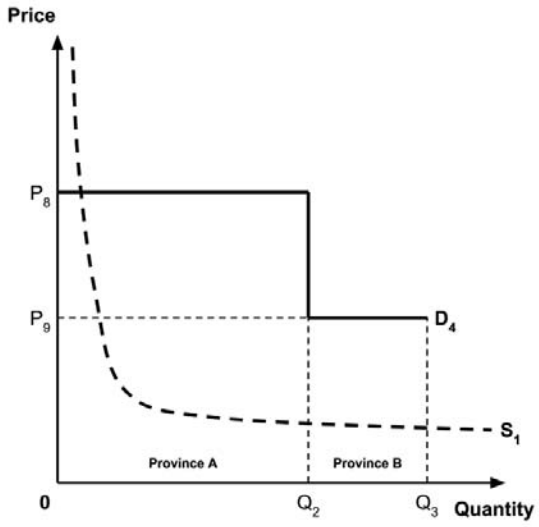


**Figure 7A: The demand curve for a medicine across two provinces**

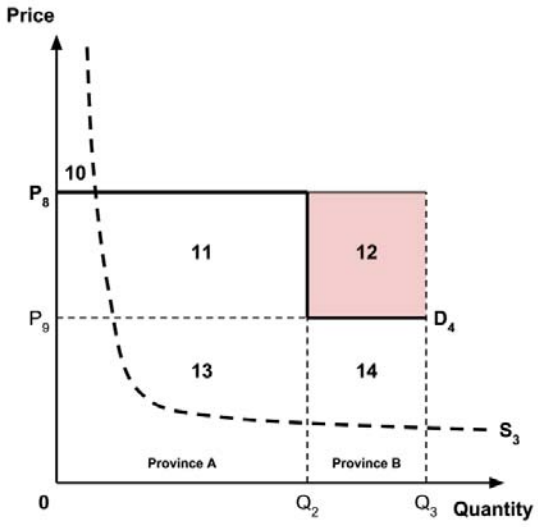


**Figure 7B: Under the first approach (ceiling price $P_8$), consumer surplus is negative in 'Province B' and zero in 'Province A', so negative overall**

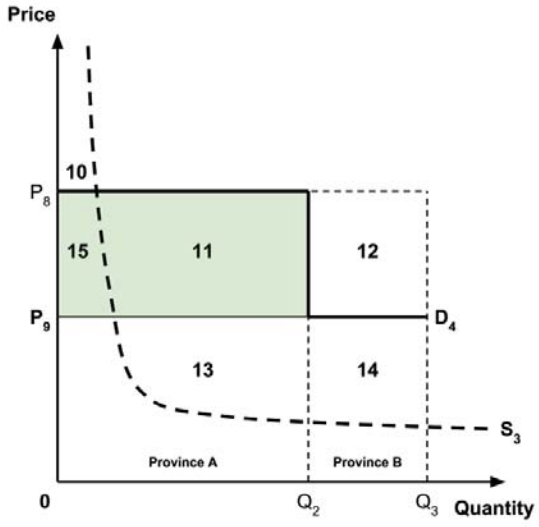


**Figure 7C: Under the second approach (ceiling price $P_9$), consumer surplus is positive in 'Province A' and zero in 'Province B', so positive overall**

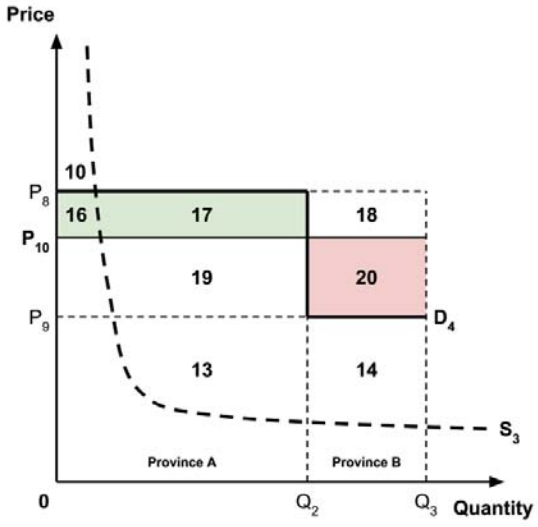


**Figure 7D: Under the third approach (ceiling price $P_{10}$), consumer surplus is positive in 'Province A'), negative in 'Province B', and zero overall**

### Approach 1: Set a ceiling price according to the highest k

Under the first approach considered by the Working Group, the ceiling price of the new medicine would be set at $P_8$ in both provinces (Figure 7B).

This would result in no consumer surplus in 'Province A' (since the ceiling price corresponds exactly to the demand curve), but negative consumer surplus in 'Province B' (as illustrated by the area of region 12) since the ceiling price lies above the demand curve. It follows that the total consumer surplus (across both provinces) would be negative, such that population health is diminished.

At this ceiling price, the producer surplus is illustrated by the combined area of regions 11, 12, 13 and 14, minus the area of region 10.

### Approach 2: Set a ceiling price according to the lowest k

Under the second approach, the ceiling price would be set at $P_9$ in both provinces (Figure 7C).

This would result in a positive consumer surplus in 'Province A' (the combined area of regions 11 and 15), and no consumer surplus in 'Province B' (since the ceiling price corresponds exactly to the demand curve), such that the total consumer surplus is positive.

The producer surplus would be lower than under the first approach, as illustrated by the combined area of regions 13 and 14, minus the combined area of regions 10 and 15.

### Approach 3: Set a ceiling price according to a weighted average of k

Under the third approach, the ceiling price would be set between $P_8$ and $P_9$ such that the total consumer surplus (across both provinces) is zero. In this example, this requires setting a ceiling price of $P_{10}$ (Figure 7D).

At a ceiling price of $P_{10}$, the positive consumer surplus in 'Province A' (combined area of regions 16 and 17) is exactly offset by the negative consumer surplus in 'Province B' (area of region 20).

The producer surplus is lower than under the first approach but greater than under the second approach, as illustrated by the combined area of regions 13, 14, 19 and 20, minus the combined area of regions 10 and 16.

## A1.3.5 Implications of a supply curve above the demand curve

In Figures 7A to 7D, the supply curve for the new medicine was plotted such that producer surplus is positive at all ceiling prices between $P_8$ and $P_9$. However, for medicines with a higher supply curve, it is possible that negative producer surplus might arise at some ceiling prices within this range.

For example, Figure 8A plots a supply curve ($S_4$) which lies entirely above $P_9$. Under the first approach considered above (pricing at $P_8$), producer surplus would be positive (the combined area of regions 22 and 23, minus the area of region 21), but the consumer surplus would be negative (as in Figure 7B). However, under the second approach (pricing at $P_9$), the medicine would have negative producer surplus (the combined area of regions 21, 24 and 25).

For medicines with a particularly high supply curve, negative producer surplus might arise at *all* ceiling prices between $P_8$ and $P_9$.

For example, Figure 8B plots a supply curve ($S_5$) which lies entirely above $P_8$. It follows that the medicine would have negative producer surplus under all of the approaches considered above, including under the first approach with a ceiling price of $P_8$ (where the negative producer surplus is illustrated by the area of region 26). In this case, no ceiling price exists which provides both positive consumer and producer surplus, as would arise in a competitive market.

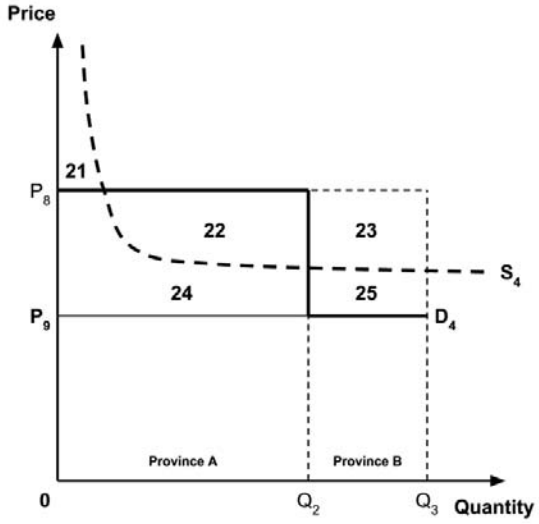


**Figure 8A: With a higher supply curve ($S_4$), the medicine is profitable at price $P_8$ but unprofitable at price $P_9$**

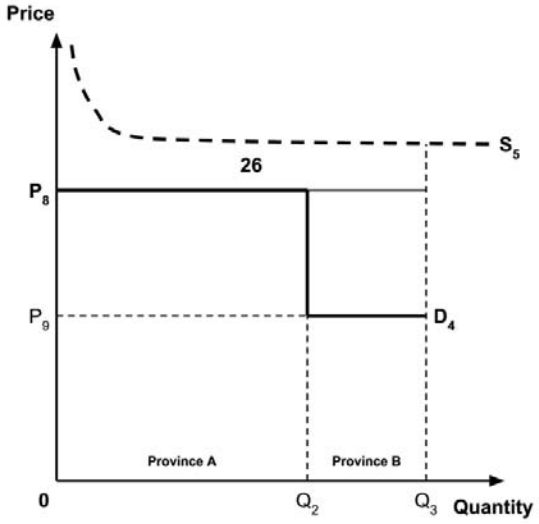


**Figure 8B: With an even higher supply curve ($S_5$), the medicine is unprofitable even at price $P_8$**

## A1.3.6 Policy implications

The most desirable approach for setting a single ceiling price across Canada depends upon the policy intent.

> *Note that it is not the role of the Working Group to specify the policy intent. While the implications of some potential policy objectives are considered below, this should not be construed as an endorsement by the Working Group of any particular policy objective. Also note that this analysis is not exhaustive: there are other potential policy objectives and approaches for setting a ceiling price across provinces and territories.*

### Potential policy objective 1

If the policy maker desires that new medicines *do not diminish population health across Canada as a whole*, such that overall consumer surplus is at least zero, then the first approach considered above is inconsistent with this policy objective. This is because this approach results in diminished population health (negative consumer surplus) in all provinces and territories except that with the highest $k$ (in which consumer surplus is zero), resulting in diminished population health (negative consumer surplus) overall.

The second approach comfortably satisfies this policy objective (since it results in positive overall consumer surplus), while the third approach only just satisfies this policy objective (since it results in an overall consumer surplus of zero).

It follows that the ceiling price that arises under the third approach ($P_{10}$ in Figure 7D) is the maximum ceiling price that would be consistent with this policy objective. At this ceiling price, overall consumer surplus is zero, analogous to the consumer surplus arising in a standard model of a monopoly with perfect price discrimination.

### Potential policy objective 2

If the policy maker instead desires that new medicines *do not diminish population health within any province or territory*, then both the first and third approaches are inconsistent with this policy objective. This is because both approaches result in diminished population health (negative consumer surplus) in at least one province or territory.

The second approach would only just satisfy this policy objective, since consumer surplus is zero in the province or territory with the lowest $k$.

It follows that the ceiling price that arises under the second approach ($P_9$ in Figure 7C) is the maximum ceiling price that would be consistent with this policy objective. Provided that producer

surplus is positive, such that the new medicine is launched, overall consumer surplus is also positive.

Note that if producer surplus is negative at $P_9$ then it is not possible to set a ceiling price which satisfies this policy objective and provides for positive producer surplus.

### Potential policy objective 3

If the policy maker wishes to set ceiling prices for new medicines so as to *maximize population health across Canada as a whole*, then consideration should be given to the location of the supply curve. Since the location of the supply curve is uncertain, this is challenging in practice.

A key assumption in the analysis below is that a medicine will not be launched if producer surplus is negative. If a medicine is not launched, the pharmacoeconomic value is zero since there is no resulting net gain in QALYs. For the pharmacoeconomic value to be positive, the medicine must be launched at a ceiling price that results in positive consumer surplus.

> The PMPRB clarified to the Working Group that its mandate is to *protect consumers from excessive pricing*, and *not* to ensure that products are launched into the market.

If the supply curve is understood to be sufficiently high that the medicine would not be profitable at the ceiling price arising under the third approach ($P_{10}$ in Figure 7D), then it is not possible to specify a ceiling price at which the medicine is profitable and improves population health.

Alternatively, if the medicine is profitable at the ceiling price arising under the third approach ($P_{10}$ in Figure 7D), but is not profitable at the ceiling price arising under under the second approach ($P_9$ in Figure 7C), then maximizing population health requires specifying a ceiling price somewhere between $P_9$ and $P_{10}$, such that consumer surplus is maximized subject to producer surplus being non-negative.

Finally, if the supply curve is understood to be sufficiently low that the medicine would be profitable at the ceiling price arising under the second approach ($P_9$ in Figure 7C), then maximizing population health requires setting a ceiling price *below* $P_9$, so as to maximize consumer surplus subject to producer surplus being non-negative. However, since the true location of the supply curve is uncertain, any reduction in the ceiling price carries a risk that producer surplus might become negative, such that the medicine would not launch at all. In such circumstances, consumer surplus would be zero, whereas at a higher ceiling price of $P_9$ the new medicine would have launched and consumer surplus would have been positive.

## A1.4 Pricing across indications

Where a medicine is available for multiple indications, this has implications for specification of the demand curve for a new medicine.

If the per-patient health gain from the new medicine is different in each indication, then the ceiling price at which the ICER is equal to $k$ will also differ across indications.

It follows that the demand curve will generally be different for each indication, with a relatively higher ceiling price corresponding to an ICER of $k$ for those indications in which the medicine has a relatively greater per-patient health gain.

### A1.4.1 Approaches for setting a single ceiling price across indications

Although the Working Group agreed that a different ceiling price should be specified for each indication *in principle*, concerns were raised about the feasibility of doing this in Canada at the present time. The Working Group therefore considered various approaches for setting a single ceiling price across multiple indications, including:

1. A ceiling price at which the medicine is 'just' cost-effective in the most cost-effective indication (such that the ICER equals $k$ in this indication);
2. A ceiling price at which the medicine is 'just' cost-effective in the least cost-effective indication;
3. A ceiling price at which the medicine is 'just' cost-effective across all indications (such that a 'weighted average' of the ICER across all indications equals $k$);
4. A ceiling price at which the medicine is 'just' cost-effective in the first indication considered by the PMPRB (such that the ICER equals $k$ in this indication).

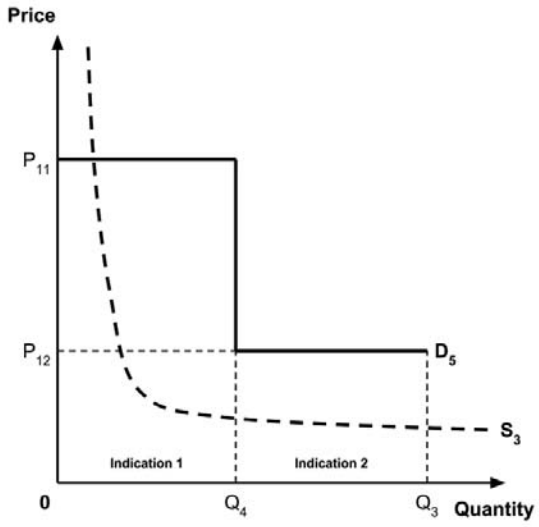


**Figure 9A: The demand curve for a medicine across two indications**

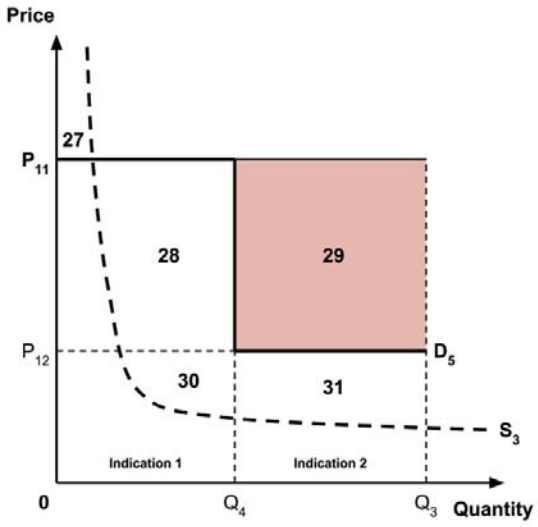


**Figure 9B: Under the first approach (ceiling price $P_{11}$), consumer surplus is negative in 'Indication 2' and zero in 'Indication 1', so negative overall**

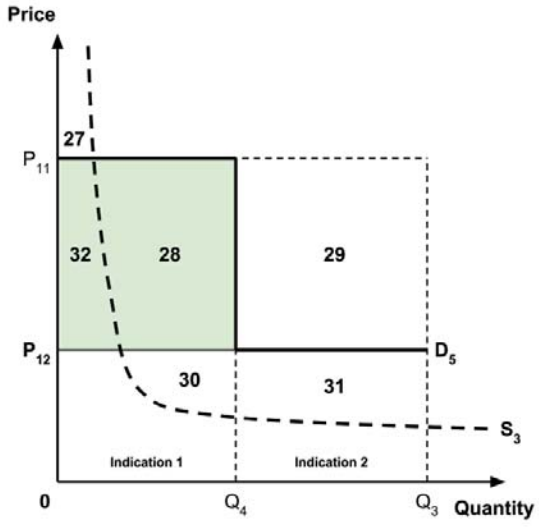


**Figure 9C: Under the second approach (ceiling price $P_{12}$), consumer surplus is positive in 'Indication 1' and zero in 'Indication 2', so positive overall**

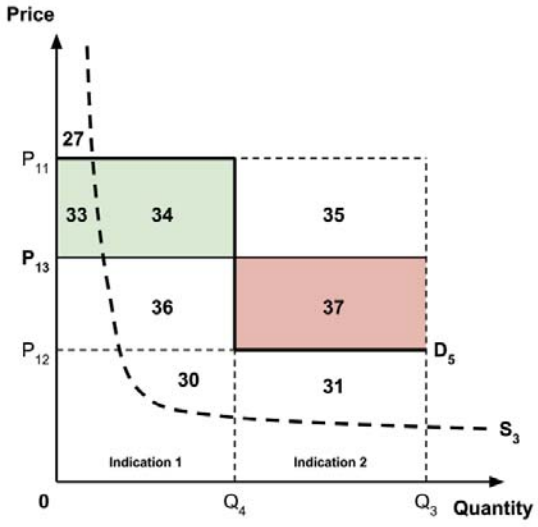


**Figure 9D: Under the third approach (ceiling price $P_{13}$), consumer surplus is positive in 'Indication 1', negative in 'Indication 2', and zero overall**

Figures 9A to 9D demonstrate the implications of each of these approaches using a simplified model of a new medicine provided to patients across two indications. In this model, the medicine is relatively more effective for patients in 'Indication 1', resulting in a larger health gain. Given this effectiveness, the ceiling price at which the ICER equals $k$ for patients in 'Indication 1' is $P_{11}$. The quantity of medicine demanded by patients in 'Indication 1' is $Q_4$. The medicine is relatively less effective for patients in 'Indication 2', such that the ICER equals $k$ at a lower ceiling price of $P_{12}$. The quantity of medicine demanded by patients in 'Indication 2' is $Q_3$ - $Q_4$.

In the analysis below, it is assumed that the medicine is always launched in both indications (i.e. the manufacturer does not strategically limit launch of the medicine to only one indication). The possible implications of such strategic behaviour are considered later in this section.

### Approach 1: Set a ceiling price based on the most cost-effective indication

Under the first approach considered by the Working Group, the ceiling price of the new medicine would be set at $P_{11}$ across both indications (Figure 9B).

This would result in no consumer surplus in 'Indication 1' (since the ceiling price corresponds exactly to the demand curve), but negative consumer surplus in 'Indication 2' (as illustrated by the area of region 29) since the ceiling price lies above the demand curve. It follows that the total consumer surplus across both indications would be negative, such that population health is diminished.

At this ceiling price, the producer surplus is illustrated by the combined area of regions 28 to 31, minus the area of region 27.

### Approach 2: Set a ceiling price based on the least cost-effective indication

Under the second approach, the ceiling price would be set at $P_{12}$ in both indications (Figure 9C).

This would result in a positive consumer surplus in 'Indication 1' (regions 28 and 32), and no consumer surplus in 'Indication 2' (since the ceiling price corresponds exactly to the demand curve), such that the total consumer surplus is positive.

The producer surplus would be lower than under the first approach, as illustrated by the combined area of regions 30 and 31, minus the combined area of regions 27 and 32.

### Approach 3: Set a ceiling price based on a 'weighted average' of all indications

Under the third approach, the ceiling price would be set between $P_{11}$ and $P_{12}$ such that the total consumer surplus (across both indications) is zero. In this example, this requires setting a ceiling price of $P_{13}$ (Figure 9D).

At this ceiling price, the positive consumer surplus in 'Indication 1' (combined area of regions 33 and 34) is exactly offset by the negative consumer surplus in 'Indication 2' (area of region 37).

The producer surplus is lower than under the first approach but greater than under the second approach (as illustrated by the combined area of regions 30, 31, 36 and 37, minus the combined area of regions 27 and 33).

### Approach 4: Set a ceiling price based on the first indication considered

Under the fourth approach, the ceiling price would be set at either $P_{11}$ or $P_{12}$, depending upon which indication is first considered by the PMPRB.

This approach is the simplest to administer, since it does not require rebenching of ceiling prices in future if and when additional indications are launched.

However, because producer surplus is unambiguously greater at a ceiling price of $P_{11}$ than $P_{12}$, this approach provides an incentive for the manufacturer to launch in the most cost-effective indication first (in this case 'Indication 1') to secure a higher ceiling price for future indications.

(If the manufacturer instead launches in 'Indication 2' first, then the loss in producer surplus is illustrated by the combined area of regions 28, 29 and 32 on Figure 9C.)

If manufacturers act upon this incentive and prioritize launch of the most cost-effective indication first, then overall consumer surplus will be zero within the initial indication and become negative once additional indications are launched. If manufacturers are perfectly strategic, then this approach would have the same implications for consumer surplus as Approach 1.

If manufacturers do *not* act upon this incentive, then in some cases consumer surplus from additional indications will be positive (if a less cost-effective indication is launched first) and in other cases consumer surplus from additional indications will be negative (if a more cost-effective indication is launched first). If the decision as to which indication to launch first is truly random, then a reasonable expectation would be that the *expected* consumer surplus associated with additional indications is zero, since it is equally likely to be positive or negative. This would have equivalent implications for consumer surplus as Approach 3.

It follows that this approach may be considered as lying somewhere between Approach 1 and Approach 3, with expected consumer surplus ranging between negative (if manufacturers are in any way strategic) to zero (if manufacturers are not strategic at all).

### A1.4.2 Similarities to pricing across multiple provinces and territories

There are several similarities between the Working Group's considerations regarding pricing across multiple indications and those regarding pricing across multiple provinces and territories.

In both cases, the demand curve for a medicine differs across subsets of patients who receive a medicine, whether on the basis of province or territory or on the basis of disease indication. In both cases, the Working Group considered pricing according to the highest or lowest of these demand curves, or pricing according to a 'weighted average' approach. And in both cases, these various approaches resulted in very different implications for the allocation of consumer and producer surplus (with one approach resulting in negative consumer surplus, another resulting in positive consumer surplus, and a third approach resulting in zero consumer surplus).

There are, however, some distinctions. First, the reason why demand curves differ across provinces or territories (because $k$ varies for a given $\Delta H$) is different from why demand curves differ across indications (because $\Delta H$ varies for a given $k$). Second, the manufacturer may have an opportunity to behave strategically regarding the order in which indications are launched, or may choose not to launch in a specific indication at all, in order to maximize profits.

### A1.4.3 Potential for strategic behaviour by manufacturers

Since manufacturers may choose not to launch in one or more indications, any approach for setting ceiling prices across indications can potentially induce strategic behaviour by manufacturers, with implications for the allocation of consumer and producer surplus.

In the earlier analysis of each of the four approaches for pricing across indications, it was assumed that the new medicine would always be launched in both indications. Under the second approach, launch of the medicine in 'Indication 2' resulted in a lower ceiling price in 'Indication 1', in turn leading to positive consumer surplus. However, if this approach were to be adopted in practice, manufacturers might strategically choose *not* to launch in 'Indication 2', resulting in a higher ceiling price for 'Indication 1', in turn leading to zero consumer surplus.

The reasons for this can be seen by considering Figure 10, which is adapted from Figure 9C. If the manufacturer launches in both indications then the ceiling price is $P_{12}$ (based on the demand curve for 'Indication 2', the least cost-effective indication). The producer surplus is then the combined area of regions 30 and 31 *minus* the combined area of regions 27 and 32.

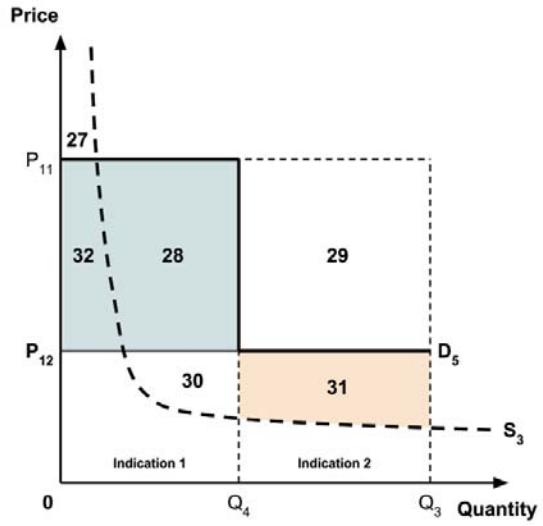


**Figure 10: Under Approach 2, the manufacturer may strategically choose *not* to launch in Indication 2, thereby increasing producer surplus by the area of regions 28 and 32 *minus* region 31**

However, if the manufacturer instead launches only in 'Indication 1', then this would now be the least cost-effective indication and so the ceiling price would be $P_{11}$. The producer surplus would now be the combined area of regions 28 and 30 *minus* the area of region 27.

It follows that, by avoiding launching in 'Indication 2', the manufacturer forgoes the producer surplus in region 31 but gains additional producer surplus in regions 28 and 32. In the example given in Figure 10, this gain in producer surplus outweighs the loss. A manufacturer wishing to maximize producer surplus would therefore strategically launch in 'Indication 1' only.

This strategic behaviour has several implications. First, it increases the producer surplus. Second, it reduces the consumer surplus (in this case to zero, although in an example with many indications the consumer surplus may be positive if the medicine still launches in two or more indications). Third, it results in a 'deadweight loss', represented by the area of region 31.

This deadweight loss arises because there is a demand for the medicine for patients in 'Indication 2', with a willingness-to-pay of $P_{12}$, and the manufacturer is willing to supply to these patients at a ceiling price lower than this. It follows that there is an economic surplus to be realized by providing the medicine to patients in 'Indication 2'. However, the manufacturer is unwilling to supply to these patients because, by doing so, the total surplus allocated to the manufacturer falls (since the ceiling price would fall from $P_{11}$ to $P_{12}$ in both indications). The potential economic surplus in region 31 is therefore not realized.

There are several potential ways to address this issue, each with positives and negatives. Applying a different ceiling price to each indication, such that the ceiling price for 'Indication 1' is independent of the ceiling price for 'Indication 2', would remove the incentive not to supply to 'Indication 2'. However, as noted earlier, members of the Working Group expressed concerns about the feasibility of implementing indication-specific pricing at the present time. Also, unless a ceiling price below the respective demand curve was applied in each indication, overall consumer surplus would be zero (analogous to that in a standard model of a monopoly with perfect price discrimination).

The policy maker might also consider applying a ceiling price higher than $P_{12}$ if the medicine is launched in both indications. In order for this to result in positive consumer surplus overall, this ceiling price would have to be lower than $P_{13}$ in Figure 9D (the ceiling price that arises under the third approach, in which consumer surplus is zero). Although a ceiling price between $P_{12}$ and $P_{13}$ would result in negative consumer surplus in 'Indication 2', there would still be positive consumer surplus overall, which might be considered preferable to the situation where the medicine is launched only in 'Indication 1' and consumer surplus is zero.

Another potential solution would be to 'penalize' the manufacturer for choosing not to launch in 'Indication 2' by setting a ceiling price below $P_{11}$ if the medicine is launched only in 'Indication 1'. This might result in producer surplus being maximized by launching in both indications, incentivising the manufacturer to also launch in 'Indication 2'. However, if the overall producer surplus becomes negative as a result of this lower ceiling price, the manufacturer might choose not to launch the medicine in *any* indication, resulting in zero consumer surplus.

Regardless of the approach taken, if the policy maker attempts to mitigate this strategic behaviour by raising or lowering the ceiling price then a key challenge is determining how much higher or lower the ceiling price should be. Since the supply curve is uncertain in practice, it is difficult to provide guidance on how much to raise or lower the ceiling price in any given case.

### A1.4.4 Policy implications

In common with the considerations made earlier regarding the setting of a single ceiling price across provinces and territories, the most desirable approach for setting a single ceiling price across indications depends upon the policy intent.

*Note that it is not the role of the Working Group to specify the policy intent. While the implications of some potential policy objectives are considered below, this should not be construed as an endorsement by the Working Group of any particular policy objective. Also note that this analysis is not exhaustive: there are other potential policy objectives and approaches for setting a ceiling price across indications.*

#### Potential policy objective 1

If the policy maker desires that new medicines *do not diminish population health across Canada as a whole*, such that overall consumer surplus is at least zero, then the first approach considered above is inconsistent with this policy objective. This is because this approach results in diminished population health (negative consumer surplus) in all indications except that which is the most cost-effective (in which consumer surplus is zero), resulting in diminished population health (negative consumer surplus) overall.

The second approach comfortably satisfies this policy objective (since it results is positive overall consumer surplus), while the third approach only just satisfies this policy objective (since it results in an overall consumer surplus of zero). The fourth approach *might* satisfy this policy objective if manufacturers are not strategic, but if manufacturers behave strategically then the *expectation* would be that consumer surplus is negative overall, in which case this approach would not satisfy this objective.

It follows that the ceiling price that arises under the third approach ($P_{13}$ in Figure 9D) is the maximum ceiling price that would be consistent with this policy objective. At this ceiling price, overall consumer surplus is zero, analogous to the consumer surplus arising in a standard model of a monopoly with perfect price discrimination.

#### Potential policy objective 2

If the policy maker instead desires that new medicines *do not diminish population health within any specific indication*, then both the first and third approaches are inconsistent with this policy objective. This is because both approaches result in diminished population health (negative consumer surplus) in at least one indication. Unless manufacturers consistently launch in the least-effective indication first, the fourth approach is also inconsistent with this objective.

The second approach would only just satisfy this policy objective, since consumer surplus is zero in the least cost-effective indication.

It follows that the ceiling price that arises under the second approach ($P_{12}$ in Figure 9C) is the maximum ceiling price that is consistent with this policy objective.

### Potential policy objective 3

If the policy maker wishes to set ceiling prices for new medicines so as to *maximize population health across Canada as a whole*, then (in common with the earlier consideration of this policy objective when pricing across provinces and territories) consideration should be given to the location of the supply curve.

As before, a key assumption is that a medicine will not be launched if producer surplus is negative. If a medicine is not launched, the pharmacoeconomic value is zero since there is no resulting net gain in QALYs. For the pharmacoeconomic value to be positive, the medicine must be launched at a ceiling price that results in positive consumer surplus.

Also as before, the most desirable ceiling price under this policy objective is the lowest ceiling price at which producer surplus is non-zero. Depending upon the location of the supply curve, this might be at a ceiling price below $P_{12}$ in Figure 9D, leading to greater consumer surplus than that resulting from any of the four approaches considered above. However, as before, lowering the ceiling price to extract additional consumer surplus carries a risk that producer surplus may become negative, such that the medicine is not launched and consumer surplus is zero.

The highest ceiling price that should be considered under this objective is that which arises under the third approach, $P_{13}$ in Figure 9D, since consumer surplus is zero at this ceiling price (analogous to a standard model of a monopoly with perfect price discrimination).

## A1.5 Uncertainty

This framework has so far assumed that $\Delta H$, $\Delta C$ and $k$ are known with certainty, such that a demand curve can be plotted at a fixed ceiling price within each province/territory and indication.

In practice, the estimates of $\Delta H$ and $\Delta C$ arising from probabilistic analyses conducted by CADTH and INESSS are uncertain, and hence the ICER of the new medicine is uncertain. Furthermore, since $k$ is subject to empirical estimation, this will also be uncertain.

### A1.5.1 Implications for the demand curve

Since both the ICER and $k$ are uncertain, the ceiling price at which the ICER is equal to $k$, and hence the location of the demand curve, is also uncertain.

Nevertheless, since CADTH now mandates the use of probabilistic analysis, the analysis output may be used to assign probability distributions to $\Delta H$ and $\Delta C$. Similarly, empirical work should allow for a probability distribution to be assigned to $k$ (see, for example, Claxton *et al.* 2015).[10] It follows that it should be possible to assign a probability distribution to the demand curve.

Figure 11 reproduces the demand curve from Figure 1 with a 95% credible interval. In this example, given uncertainty in $\Delta H$, $\Delta C$ and $k$, the net health benefit (consumer surplus) of the medicine is *expected* to be zero at a ceiling price of $P_1$ (illustrated by the 'mean' demand curve). Given this uncertainty, there is a 95% probability that the net health benefit is *actually* zero at a ceiling price between $P_{14}$ and $P_{15}$ (illustrated by the 'U 95%' and 'L 95%' demand curves).

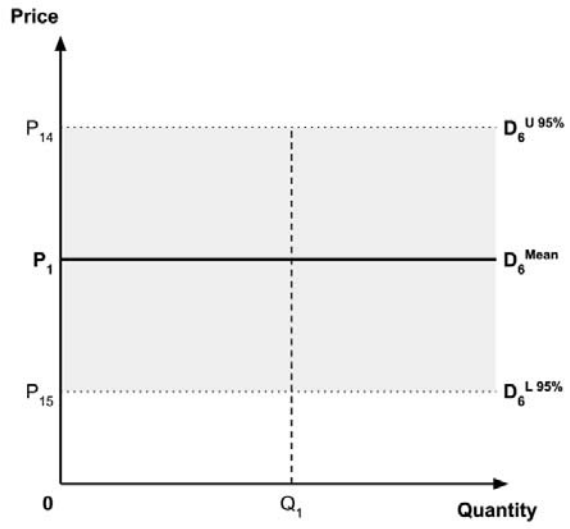


**Figure 11: Demand curve subject to a 95% credible interval**

## A1.5.2 Expected loss in economic surplus

Since the ceiling price at which the net health benefit (consumer surplus) of the medicine is *actually* zero is uncertain, there is a possibility that the ceiling price at which a new medicine is *expected* to provide zero consumer surplus ($P_1$ in Figure 11) will *actually* result in positive consumer surplus, and similarly there is a possibility that this ceiling price will *actually* result in negative consumer surplus. There is also a possibility that this ceiling price will *actually* result in zero consumer surplus, which would arise if $P_1$ lies below the supply curve (such that the medicine is not launched).

Consider Figure 12A. In this example, the *actual* ceiling price at which net health benefit (consumer surplus) is zero is $P_{16}$. This is the ceiling price at which the demand curve would be plotted if $\Delta H$, $\Delta C$ and $k$ were known with certainty. Since these parameters are uncertain, the true location of this *actual* demand curve is unknown (and is plotted with a dashed line). Instead, we have an estimate of the *expected* ceiling price at which net health benefit is zero ($P_1$), and also an estimate of the 95% credible interval (between $P_{14}$ and $P_{15}$).

Suppose the PMPRB specifies a ceiling price of $P_1$, based on the *expected* (mean) demand curve. Because $P_1$ is lower than the (unknown) *actual* demand curve, but above the (unknown) supply curve at quantity $Q^1$, it follows that a ceiling price of $P_1$ will result in a positive consumer surplus (illustrated by the combined area of regions 34, 35 and 36). Producer surplus will also be positive (illustrated by the combined area of regions 37 and 38, minus the combined area of regions 33 and 34), but lower than it would have been if the ceiling price were set according to the *actual* demand curve (with the reduction in producer surplus equal to the gain in consumer surplus). Critically, because producer surplus is positive at $P_1$, the medicine is still launched. It follows that, *in this example*, uncertainty has resulted in a *positive* consumer surplus.

Now consider Figure 12B. In this example, the *actual* demand curve ($P_{17}$) lies *below* the expected (mean) demand curve ($P_1$). It follows that, if the medicine is adopted at a ceiling price $P_1$, then consumer surplus will be *negative* (illustrated by the combined area of regions 40, 41 and 42), since a higher ceiling price is paid than that at which consumer surplus is zero. Producer surplus is greater than it would have been in the absence of uncertainty (illustrated by the combined area of regions 41 to 44, minus the area of region 39), with this gain in producer surplus equal to the reduction in consumer surplus (illustrated by the combined area of regions 40, 41 and 42).

This brings us to a key result. Provided that the medicine is launched at a ceiling price coinciding with the *expected* demand curve (a crucial requirement considered further below), the *expected* consumer surplus is zero (analogous with a model of a monopoly with perfect price discrimination). The *actual* consumer surplus may be positive (as in Figure 12A) or negative (as in Figure 12B), but the *expected* consumer surplus is zero.

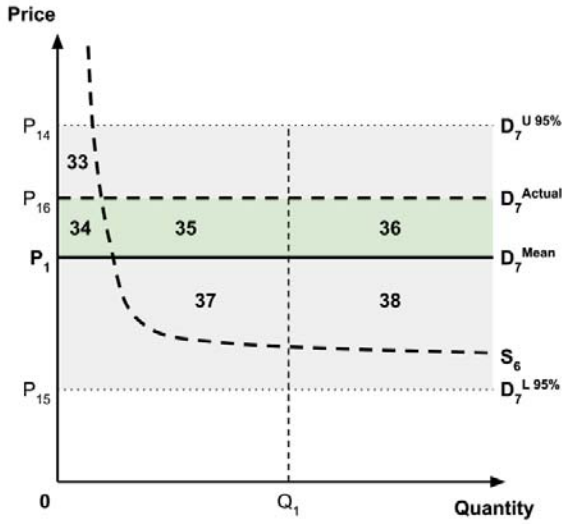


**Figure 12A: Example where the actual demand curve ($P_{16}$) lies *above* the expected demand curve ($P_1$) and the medicine is launched**

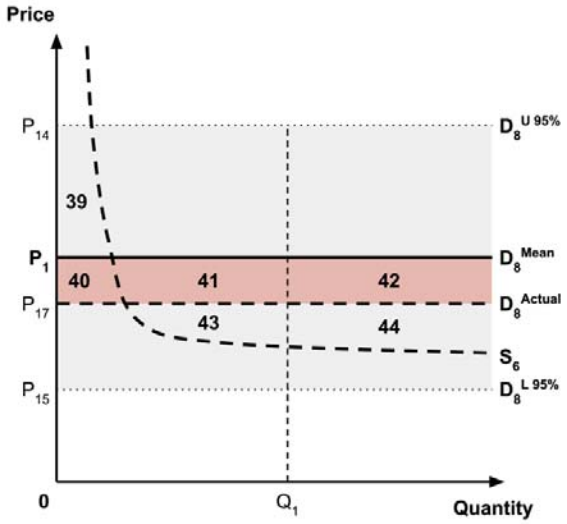


**Figure 12B: Example where the actual demand curve ($P_{17}$) lies *below* the expected demand curve ($P_1$) and the medicine is launched**

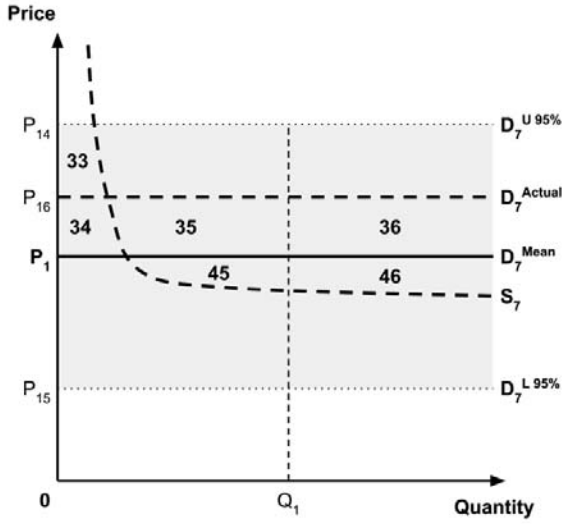


**Figure 12C: Example where the actual demand curve ($P_{16}$) lies *above* the expected demand curve ($P_1$) and the medicine is *not* launched**

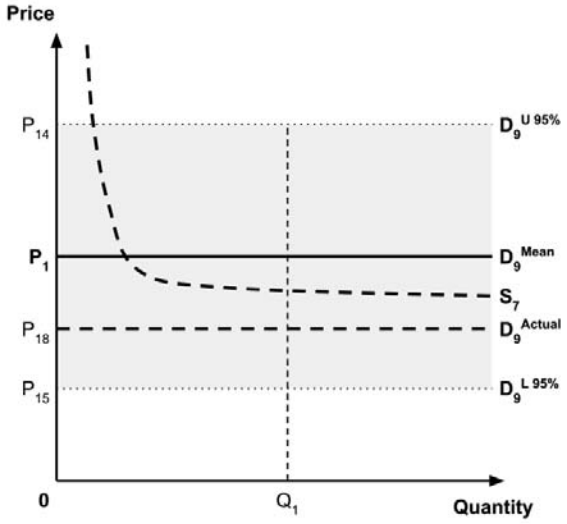


**Figure 12D: Example where the actual demand curve ($P_{18}$) lies *below* the expected demand curve ($P_1$) and the medicine is *not* launched**

However, this result does not hold if the medicine is *not launched* as a result of uncertainty.

Consider Figure 12C. In this example, the *actual* and *expected* demand curves are identical to those in Figure 12A, but the supply curve is now higher ($S_7$). If the ceiling price coinciding with the *actual* demand curve ($P_{16}$) were known in practice and offered to the manufacturer, then the medicine would be launched since the producer surplus would be positive (illustrated by the combined area of regions 35, 36, 45 and 46, minus the area of region 33). However, this is not possible because the *actual* demand curve is unknown. If the manufacturer is instead offered the ceiling price coinciding with the *expected* demand curve ($P_1$), then the manufacturer will choose *not* to launch the medicine, because the producer surplus would now be negative (illustrated by the combined area of regions 45 and 46, minus the combined area of regions 33 and 34). Since the producer surplus would be negative, and so the medicine is not launched, it follows that both the consumer surplus and producer surplus are zero. Compared to Figure 12A, in which both consumer and producer surplus were positive since the medicine still launched, in this example the uncertainty results in a loss of economic surplus (with the total loss illustrated by the combined area of regions 35, 36, 45 and 46, minus the area of region 33).

Finally, consider Figure 12D. The *expected* demand curve and supply curve are identical to those in Figure 12C, so again the medicine is *not* launched because it would have negative producer surplus. However, in this example the *actual* demand curve ($P_{18}$) is lower than the *expected* demand curve ($P_1$). As a result, the medicine would not have launched anyway in the absence of uncertainty, such that the uncertainty does *not* result in a loss in economic surplus (since there would have been none anyway).

To summarize the results from the examples above:

1. If the medicine is launched at a ceiling price coinciding with the *expected* demand curve then the *expected* consumer and producer surplus is zero.

2. If the medicine is unprofitable at a ceiling price coinciding with the *expected* demand curve, and is *also* unprofitable at a ceiling price coinciding with the *actual* demand curve, then the consumer surplus is zero.

3. If the medicine is unprofitable at a ceiling price coinciding with the *expected* demand curve, but would have been profitable at a ceiling price coinciding with the *actual* demand curve, then the impact of uncertainty is to *diminish* the total economic surplus such that *expected* consumer surplus at a ceiling price coinciding with the expected demand curve is *negative*.

It follows from this third result that uncertainty is associated with an expected loss in consumer surplus, such that reducing uncertainty results in an expected gain in consumer surplus.

## A1.6 Market size

The PMPRB has proposed that a 'market size adjustment' may be applied to the ceiling price for some Category 1 medicines. This includes a potential upwards ceiling price adjustment for medicines with small market size and, independently, a potential downwards ceiling price adjustment for medicines with large market size.

The first of these would have the effect of increasing the producer surplus (at the expense of consumer surplus) for medicines with small market size. The second would increase the consumer surplus (at the expense of producer surplus) for medicines with large market size.

Consider Figure 13A, which reproduces the demand and supply curves for a hypothetical new medicine from Figure 4A.

For simplicity, it is assumed that the medicine has a single indication and there are no differences in $k$ across provinces and territories, such that there is a single horizontal demand curve ($D_1$) at a ceiling price of $P_1$. It is also assumed that the ceiling price of the medicine is $P_1$, such that consumer surplus is zero (in the absence of a market size adjustment).


**Figure 13A: Without any 'market size adjustment'**

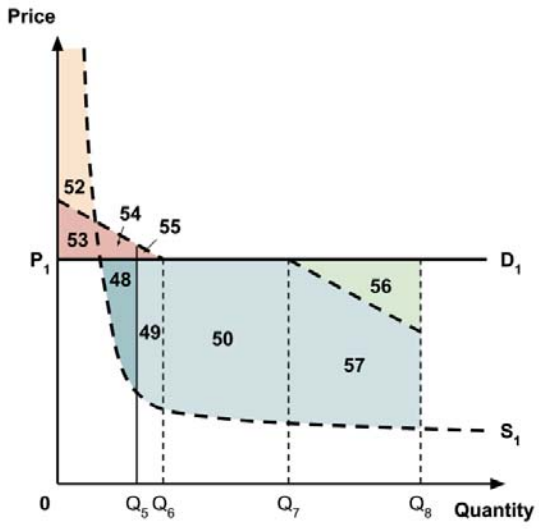


**Figure 13B: With a hypothetical 'market size adjustment'**

If this medicine has very small market size (quantity $Q_5$), then it will have negative producer surplus (as illustrated by the area of region 48 minus the area of region 47), such that it would not be profitable to launch. If the medicine has slightly larger market size ($Q_6$), then the producer surplus increases (by the area of region 49) but is now zero, such that the manufacturer is ambivalent about launching the medicine. With even larger market size ($Q_7$), the producer surplus increases further (by the area of region 50), such that the medicine is now profitable. And with the largest market size ($Q_8$), the medicine has an even greater producer surplus (as illustrated by the combined area of regions 48, 49, 50 and 51, minus the area of region 47).

Note that $Q_6$ is the minimum market size at which the medicine is profitable. A smaller market size results in negative producer surplus, while a larger market size results in increasingly positive producer surplus.

### A1.6.1 Implications of a market size adjustment

Now consider Figure 13B, which illustrates a hypothetical ‘market size adjustment’. Following this market size adjustment, medicines with market size below $Q_6$ receive a higher ceiling price, while medicines with market size above $Q_7$ receive a lower ceiling price.

In order to allow for comparisons between medicines with small and large market size, it will now be assumed that there are many new medicines, each with identical demand and supply curves as plotted in Figure 13B, with these medicines differing in terms of their market size.

This hypothetical market size adjustment has a number of implications.

#### Implication 1: Increased consumer surplus from medicines with large market size

The reduction in the ceiling price for medicines with large market size results in an increase in consumer surplus (as illustrated by the area of region 56 for a medicine with market size $Q_8$).

Producer surplus for medicines with large market size is reduced by an equivalent amount, but remains positive because it was sufficiently large prior to the reduction in ceiling price.

Since the market size adjustment did not cause the demand curve to cross the supply curve, the producer surplus for a medicine with market size $Q_8$ remains larger than the producer surplus at any smaller market size (as illustrated by the combined area of regions 48, 49, 50 and 57, minus the combined area of regions 52 and 53).

#### Implication 2: Reduced consumer surplus from medicines with small market size

A higher ceiling price for medicines with small market size results in greater producer surplus (as illustrated by the combined area of regions 53, 54 and 55), but a correspondingly lower consumer surplus.

Since (in this example) consumer surplus was zero prior to the market size adjustment, it follows that consumer surplus is now negative for medicines with small market size.

### Implication 3: Increased profitability for medicines with small market size

For a medicine with a market size of $Q_5$, the producer surplus following the market size adjustment is zero (as illustrated by the area of regions 48, 53 and 54, minus the area of region 52), where previously it was negative.

For a medicine with a market size of $Q_6$, the producer surplus is now positive (as illustrated by the combined area of regions 48, 49, 53, 54 and 55, minus the area of region 52), where previously it was zero.

It follows that the minimum market size at which a medicine is profitable has fallen from $Q_6$ (prior to the market size adjustment) to $Q_7$. Medicines with a market size between $Q_5$ and $Q_6$, which were unprofitable prior to the market size adjustment, now have positive producer surplus. This might, in turn, result in greater access to medicines with small market size.

# Appendix 2: Materials Presented at Meetings of the Working Group

# Appendix 2.1: Slides from 26 July 2018 (Dr Mike Paulden)

# Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines

Alt Hotel, Ottawa, ON
26 July 2018

Chair: Dr Mike Paulden

## Background

*The Patented Medicine Prices Review Board (PMPRB) recently established a 'Steering Committee on Modernization of Price Review Process Guidelines'.*

*The mandate of this Steering Committee is to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of the PMPRB's new draft Guidelines.*

*The Steering Committee's work will be based in part on the analysis and recommendations of a technical Working Group, which will examine certain issues that the Steering Committee believes would benefit from the review of experts in health technology assessment and other economic and scientific matters.*

# Background

*The Working Group will comprise leading experts in pharmacoeconomics and the clinical evaluation of pharmaceuticals.*

*The Working Group will meet four times between July and October 2018: twice in-person in Ottawa, and twice via video-conference.*

*A report of the Working Group's deliberations and recommendations will be produced by the chair and submitted to the Steering Committee for consideration in October 2018.*

# Members

*1. Dr Chris Cameron (Dalhousie University and Cornerstone Research Group);*

*2. Dr Tammy Clifford (University of Ottawa and CADTH);*

*3. Dr Doug Coyle (University of Ottawa);*

*4. Patrick Duford (INESSS);*

*5. Don Husereau (Institute of Health Economics);*

*6. Dr Peter Jamieson (University of Calgary);*

*7. Dr Frédérick Lavoie (Pfizer Canada);*

*8. Dr Karen Lee (University of Ottawa and CADTH);*

*9. Dr Christopher McCabe (University of Alberta and Institute of Health Economics);*

*10. Dr Stuart Peacock (Simon Fraser University and BC Cancer Agency);*

*11. Maureen Smith (Patient – Health Quality Ontario);*

*12. Geoff Sprang (Agmen);*

*13. Dr Tania Stafinski (University of Alberta).*

# Observers and Reviewers

***Observers***

*1. Edward Burrows (Innovation, Science and Economic Development);*

*2. Nelson Millar (Health Canada).*

***External reviewer***

*1. Dr Mark Sculpher (University of York).*

# Confidentiality

*Working Group members may consult with non-members on an ongoing basis but are expected to maintain the confidentiality of any materials provided to them during the course of their work.*

*The names of the members of the Working Group will be published on the PMPRB's website, along with a report of its deliberations, analysis and recommendations.*

# Governance and procedure

*It is recognized that members of the Working Group may hold opposing points of view on the above issues and/or disagree with the policy rationale underlying the changes to the PMPRB's Guidelines.*

*Members are nonetheless encouraged to work together constructively to assist the Working Group in carrying out its function.*

# Governance and procedure

*The chair is expected to foster consensus among members, but in order to ensure that Working Group deliberations are as focused and productive as possible, the chair shall have final say on all matters of governance and procedure.*

*Members who disagree with a decision of the chair in this regard can request that their objection be noted on the record.*

*The chair shall make every effort to ensure that the Working Group's final report accurately reflects any important points of convergence or contention between members.*

# Schedule

| Date | Event | Purpose |
|---|---|---|
| 26 July 2018 | Full day in-person meeting in Ottawa | Overview of Working Group objectives. Summary of specific areas of focus under consideration. Allocation of tasks among Working Group members. |
| Week of 20 August 2018 (TBC) | Two hour video-conference | Update on Working Group status. Opportunity for input from Working Group members. |
| Week of 10 September 2018 (TBC) | Two hour video-conference | Update on Working Group status. Opportunity for input from Working Group members. |
| 5 October 2018 | Draft report submitted to PMPRB | Opportunity for input from PMPRB and Working Group members. |
| 12 October 2018 | Full day in-person meeting in Ottawa | Present draft report. Report draft recommendations.<br>Final opportunity for input from PMPRB and Working Group members. |
| 26 October 2018 | Final report delivered to PMPRB | Final deliverable to PMPRB. |

# Deliverables

*A draft report will be circulated to the Steering Committee and Working Group members on 5 October 2018, prior to the final in-person meeting in Ottawa.*

*Following delivery of the final report, the chair will be willing to present the recommendations of the Working Group to stakeholders and other interested parties, subject to availability.*

# Background and Overview

# Group discussion

# Areas of focus

1. Options for determining what drugs fall into 'Category 1'
2. Application of supply-side cost effectiveness thresholds in setting ceiling prices for Category 1 drugs
3. Drugs with multiple indications
4. Options for using the CADTH and/or INESS reference case analyses to set a ceiling price
5. Perspectives
6. Application of the market size factor in setting ceiling prices

# 1. Options for determining what drugs fall into 'Category 1'

*A Category 1 drug is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing.*

*The following criteria have been identified as supporting a Category 1 classification:*

*a) The drug is 'first in class' or a 'substantial' improvement over existing options*

*b) The drug's opportunity cost exceeds its expected health gain*

*c) The drug is expected to have a high market impact*

*d) The drug has a high average annual treatment cost*

**Should other criteria be considered?**

**What are the relevant metrics for selecting drugs that meet the identified criteria and what options exist for using these metrics?**

# 2. Application of supply-side cost effectiveness thresholds in setting ceiling prices for Category 1 drugs

*Potential approaches for implementing a price ceiling based on a drug's opportunity cost.*

*Potential approaches for allowing price ceilings above opportunity cost based on a higher willingness to pay for certain types of drugs (e.g. pediatric, rare, oncology, etc)*

**What are the potential approaches for considering a drug's opportunity cost and implementing a price ceiling?**

**Should higher price ceiling(s) be adopted for certain types of drugs? If so, which drugs? How should the higher price ceiling(s) be determined?**

# 3. Drugs with multiple indications

*Options for addressing drugs with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).*

**What are the available options regarding pricing for multiple indications?**

**Which option should be recommended, and why?**

# 4. Accounting for uncertainty

*Options for using the CADTH and/or INESS reference case analyses to set a ceiling price.*

*Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.*

**Do existing 'reference case' analyses provide the most appropriate estimates from which to derive a ceiling price?**

**If not, what modifications from the 'reference case' assumptions are desirable?**

**How should uncertainty be accounted for, or addressed, when setting price ceilings?**

# 5. Perspectives

*Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a 'significant' difference between price ceilings under each perspective.*

*How to define a 'significant' difference in price ceilings between each perspective.*

**What are the key differences between a public health care system vs societal perspective?**

**What are the options to account for these differences?**

**How should a 'significant' difference be defined?**

# 6. Application of the market size factor in setting ceiling prices

*Approaches to derive an appropriate affordability adjustment to a drug's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' approach).*

**What approaches are available to consider an 'affordability adjustment' to a drug's ceiling price?**

**Should other factors be considered (in addition to market size and GDP)?**

**How should each of these factors be considered?**

# Closing

# Appendix 2.2: Note on Uncertainty (Dr Christopher McCabe)

# Considering uncertainty when setting a ceiling price for technologies using a cost effectiveness threshold: a note to the PMPRB Technical Working Group.

Christopher McCabe PhD,
Professor of Health Economics, Faculty of Medicine and Dentistry,
University of Alberta

CEO and Executive Director, Institute of Health Economics, Alberta

## Background

The Patented Medicines Price Review Board (PMPRB) are considering using a cost effectiveness threshold to identify a ceiling price for new patented medicines in Canada [hereafter referred to as Value Based Pricing Ceiling (VBPc)]. As part of the process for revising its review process, PMPRB has established a technical working group to comment on technical/methods issues relating to this proposal, that have been identified in the consultation process. One of the technical issues that PMPRB are seeking commentary on is the mechanisms for dealing with uncertainty in the evidence base, within analyses undertaken for VBPc. In this note, we describe the nature of the uncertainties in the evidence base and how they may be addressed analytically within the standard framework of cost effectiveness analysis, in a timely manner from the perspective of the PMPRB's objective of providing timely access to innovation.

The contents of this note should not be interpreted as providing any comment on the desirability or otherwise of VBPc in Canada. Further, the contents of this note should not be interpreted as representing the views of the Institute of Health Economics, its Board, Members or funders, on any of the issues relating to VBPc in Canada.

The remainder of this note is structured as follow: first we describe the categories of uncertainty that a VBPc process *could* consider, the constituent components of those categories and how they relate to the decision that a VPBc setting body such as PMPRB is charged with making; then we rehearse key concepts from decision science: decision uncertainty, the expected cost of making the wrong decision, value of information, and the associated concept of expected net benefit of sampling; finally we describe how these concepts could be used by PMPRB to identify a VBPc. We end with a short note on why the PMPRB (or any VBPc authority) should not considering uncertainty in the Incremental Cost Effectiveness Ratio for a specific product in setting a ceiling price.

## Categories of uncertainty potentially pertinent to VBPc process

There are two models of the cost effectiveness threshold; often referred to as the Demand side and Supply side Threshold respectively. The Demand side threshold can usefully be differentiated from the supply side threshold by labelling it the Willingness to Pay for Health. (ref) The Supply side threshold represents the value of the health displaced by the adoption of a new technology under a fixed and fully allocated health system budget. This is often referred to as the Opportunity Cost of adopting a new technology – even though this is not a technically correct use of the term Opportunity Cost. (ref). Both forms of the cost effectiveness threshold are empirical quantities, which in principle can be measured with a degree of uncertainty. For the purposes of this note, is does not matter whether the VBPc is established with reference to a Demand or Supply side threshold.

If we only know the cost effectiveness threshold with uncertainty, there is a risk that the empirical value will be higher or lower than the true value. The econometric studies that typically provide empirical estimates produce an expected value and a description of the uncertainty around that expected value via Standard Errors. These data can be used to characterise a probability distribution that describes the range of credible values for the threshold and the probability that any specific value in the credible range is the true value. This

information allows analysts to examine two important questions: (1) What is the probability that that using the estimate of the cost effectiveness threshold to set a ceiling price, we introduce a technology to the market that will displace more health than it produces, because the estimated threshold is higher than the actual threshold (Type 1 Error); and (2) What is the probability that that using the estimate of the cost effectiveness threshold to set a ceiling price, we exclude a technology from the market that would produce more health than it displaces, because the estimated threshold is lower than the actual threshold (Type 2 Error).

In addition to uncertainty regarding the true value of the cost effectiveness threshold, there is uncertainty about the true value (cost effectiveness) of the technologies. Much, although not all, of this uncertainty derives from uncertainty in the evidence base for the new technology, the technologies it is being compared to and the epidemiology and natural history of the condition that the technology targets. In this context, the evidence base includes resource use, costs and quality of life, as well as the more conventional concerns of effectiveness and safety. Uncertainty in the evidence base will contribute to (a) the risk of adopting a technology that should not be adopted because its actual cost effectiveness is above than the threshold even though the estimated cost effectiveness is below the threshold; and (b) rejecting a technology that should be accepted because its estimated cost effectiveness is greater than the threshold even though its actual cost effectiveness is below the threshold. The uncertainty regarding each component of the evidence base can be assessed from the perspective off whether resolving the uncertainty would be expected to change the decision. This is the foundational observation of Value of Information Analysis, a well established set of techniques from decision science. In the next section, we will provide a brief description of the concepts and specific applications of Value of Information Analysis.

## Decision making, uncertainty and value of information

Decisions are by definition dichotomous. We choose to do one thing and in doing so, we choose not to do the alternative. Evidence, by contrast, tends to be uncertain and thus sits on a

continuum of probability. Cost effectiveness analysis synthesises all available (and relevant) evidence to estimate the expected incremental costs and incremental effects of the new therapy compared to one or more currently used therapies. Because the evidence is not certain, the estimates of the costs and effects are drawn from distributions, which reflect the uncertainty in the evidence base pertaining to the clinical pathway patients would follow when receiving the alternative therapies, the resource use, costs and health related quality of life associated with the different components of those clinical pathways.

As indicated above, decision making using cost effectiveness analysis requires the specification of a threshold value for the incremental cost effectiveness ratio, above which the new therapy is considered poor value and below which it is considered good value. When the uncertainty in the cost effectiveness is recognised and quantified – as it is in cost effectiveness analyses that comply with good practice guidelines – we can quantify the probability that the decision based upon the expected incremental cost effectiveness ratio will be the wrong decision (either rejecting a good value therapy or accepting a poor value therapy). The probability of making the wrong decision is called the 'Decision Uncertainty'. Cost effectiveness analysis allows us to go further than simply characterising Decision Uncertainty; it allows us to attach a value to making the wrong decision. If we make the wrong decision, then we will be giving up health – by either adopting a technology that displaces more health elsewhere in the system due to its true excess cost, or by continuing to fund a technology within the health care system that actually produces less health than the new technology would if we adopted it. The cost effectiveness threshold ($s per Unit of Health gained) can be applied to the health loss associated with making the wrong decision, to quantify if the decision is wrong. The expected cost of making the wrong decision is obtained by weighting this by the probability of making the wrong decision given current evidence.

There are broadly two responses to concern about making a wrong decision given the current evidence. The first is to collect more evidence, which improves the evidence base and thereby reduces the decision uncertainty. The second is to modify to the point where the cost of making

the wrong decision is less than the cost of delaying the decision to allow more evidence to be collected. Both of these approaches can be formalised through the using the Value of Information framework. The easiest way of thinking about the value of information is as the reduction in the expected cost of making the wrong decision attributable the additional information provided research, net the cost of undertaking the research.[1] When we consider the value of the additional information provides by a specific research study and net out the cost of the research, this is referred to as the Net Benefit of Sampling.

Having reviewed these key concepts, we now turn to consider how a VBPc framework could take account of uncertainty in the value of the cost effectiveness threshold.

## Incorporating uncertainty in the value of the cost effectiveness threshold into a VBPc

We start by re-iterating that the cost effectiveness threshold is an empirical quantity that can be estimated with uncertainty, therefore we can characterize the uncertainty and its value using the methods of probabilistic analysis and value of information analysis that are recommended in the Canadian Agency for Drugs and Technologies in Health (CADTH) Guideline for Economic Evaluations: Canada. (2017).

The cost making the wrong decision with regard to uncertainty in the threshold is two-sided - setting a price that is too high because the threshold value is actually lower than the estimate leading to a loss of health; and setting the price too low leading to the technology being withheld from the market, because the actual threshold is higher than the estimate. It follows that the expected value of the wrong decision is the sum of these two factors.

[1] The definition of cost of the research includes any health gains foregone and/or harms incurred whilst the research is undertaken as well as all financial costs associated with the research.

The VBPc setting authority does not know the price that is consistent with a company's minimum willingness to accept. Given the consistent messages from all levels of government that the policy objective prioritises access to new therapies, it is appropriate for the analyst to adopt a risk averse position and assume that company's minimum willingness to pay requires only a marginal increase in the cost effectiveness threshold and thereby maximize the probability that we have incorrectly excluded them. Hence the probability of making a Type 1 error is the portion of the distribution of the threshold parameters that is above the expected value. The cost of a Type 1 error is the sum of the net benefit calculated using the range of threshold values above the expected value weighted by the probability that each value is the true value multiplied by the population that would benefit.

The cost of a Type 2 error due to threshold uncertainty is slightly different because the technology is provided but it is possible that the ceiling price is over-rewarding it. Therefore, the cost of making the wrong decision is the sum of the *difference* between the net benefit estimated using the expected threshold and each possible threshold value below the expected value, weighted by the probability that it is the actual value. This is then multiplied by the size of the patient population to get the total cost.

If the sum of the cost of these two types of error is not equal to zero, and there is no reason a priori why it should be, then the threshold should be increased or decreased to identify the value which minimizes the sum of the two effects. Theoretically, when the minimum loss identified by this process is non-zero, consideration should be given to the question of whether the cost of further research to reduce the uncertainty in the true value of the threshold is greater than the value of the uncertainty. Pragmatically this would likely not be practical, as this would be a technology specific assessment, and the desirability of consistent and timely VBPc decisions would indicate argue against such an approach. However, period reviews of the total loss attributable to uncertainty in the value of threshold across a portfolio of assessments, would provide empirical evidence on the value of further research to improve the evidence on

the cost effectiveness threshold used.

## Uncertainty in the Incremental Cost Effectiveness Ratio and VBPc

It is worth noting that there is uncertainty in the value of the technology, that this uncertainty is empirical and hence in principle can be addressed using the same concepts as outlined above. We would also note that if such an approach is adopted it should focus only on the components of the evidence base that the company could realistically influence through the design of the Research and Development programme that brought the product to market – broadly safety, effectiveness, resource utilisation and health related quality of life.

However, in the context of a VBPc framework, we argue that value of the uncertainty in the evidence base for the technology can be considered out of scope. We hold this position for two reasons. First, the function of the VBPc authority is to set a maximum price consistent with access to the market. In the form described above, we have set a specific risk attitude – averse to Type 1 errors – and this risk attitude may not be the one that health care payers wish to adopt. Health care payers have considerable experience of addressing uncertainty in the evidence base for a technology and understand their attitude to such risk and their preferred strategies for managing it. It is not obvious that there is value in the VBPc authority acting in the space.

Secondly, increasingly innovative technologies are receiving conditional licensing approval; i.e. the regulator provides temporary market access in order to allow research that will reduce the uncertainty in the evidence base for their value. If this same uncertainty were considered by the VBPc authority, this would drive down the price of the technology and reduce the likelihood that the technology would enter this market. The policies of the licensing and VBPc authorities would be in direct conflict.

3rd October 2018

# Appendix 2.3: Slides from 12 October 2018 (Dr Mike Paulden)

# Strategic Behaviour and the Cost-Effectiveness Threshold

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1

## Supply-side threshold (k)

Determined by the **opportunity cost** of **new interventions**

PharmacoEconomics
https://doi.org/10.1007/s40273-017-0585-2

ORIGINAL RESEARCH ARTICLE

**Estimating the Reference Incremental Cost-Effectiveness Ratio for the Australian Health System**

Laura Catherine Edney[1] · Hossein Haji Ali Afzali[1] · Terence Chai Cheng[2] · Jonathan Karnon[1]

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**Abstract**

*Background* Spending on new healthcare technologies increases net population health when the benefits of a new technology are greater than their opportunity costs—the benefits of the best alternative use of the additional resources required to fund a new technology.

*Objective* The objective of this study was to estimate the expected incremental cost per quality-adjusted life-year (QALY) gained of increased government health expenditure as an empirical estimate of the average opportunity costs of decisions to fund new health technologies. The estimated incremental cost-effectiveness ratio (ICER) is proposed as a reference ICER to inform value-based decision making in Australia.

*Methods* Empirical top-down approaches were used to estimate the QALY effects of government health expenditure with respect to reduced mortality and morbidity. Instrumental variable two-stage least-squares regression was used to estimate the elasticity of mortality-related QALY losses to a marginal change in government health expenditure. Regression analysis of longitudinal survey data representative of the general population was used to isolate the effects of increased government health expenditure on morbidity-related, QALY gains. Clinical judgement informed the duration of health-related quality-of-life improvement from the annual increase in government health expenditure.

*Results* The base-case reference ICER was estimated at AUD26,033 per QALY gained. Parametric uncertainty associated with the estimation of mortality- and morbidity-related QALYs generated a 95% confidence interval AUD20,758–37,667.

*Conclusion* Recent public summary documents suggest new technologies with ICERs above AUD40,000 per QALY gained are recommended for public funding. The empirical reference ICER reported in this article suggests more QALYs could be gained if resources were allocated to other forms of health spending.

**Electronic supplementary material** The online version of this article (doi:10.1007/s40273-017-0585-2) contains supplementary material, which is available to authorized users.

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Published online: 22 December 2017

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# Demand-side threshold (v)

Determined by society's **willingness-to-pay** for **improved health 'benefit'**

Journal of Health Economics

Trying to estimate a monetary value for the QALY

Jose Luis Pinto-Prades, Graham Loomes, Raul Brey

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## Additional considerations

- In practice, funding decisions involve a number of **complex considerations** which are *not* reflected by **conventional demand/supply-side thresholds**
- Funding might **displace health care services** that provide 'benefit' to other patients - *not accounted for in a demand-side approach*
- Specifying **λ** might result in **strategic pricing behaviour** from manufacturers
- Manufacturers may be **unwilling to supply new technologies** if λ is **low**, but may make **large profits** at the expense of **population health** if λ is **high**
- A decision maker interested in both **consumer** and **producer** interests may wish to understand the **trade-offs** associated with **different values of λ**



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# A new conceptual model

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## Overview

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- This paper proposes a **new conceptual model of the cost-effectiveness threshold** that incorporates these **additional considerations**
- Considers both **opportunity cost** and society's **willingness-to-pay** for health 'benefit' from conventional **supply-side** and **demand-side** approaches
- Considers **costs incurred by manufacturers** in developing technologies and the **incentive for manufacturers to strategically price up to λ**
- Allows for considerations of **'consumer surplus'** and **'producer surplus'**, so decision makers may consider **how λ impacts upon the distribution of surplus between consumers (patients) and producers (manufacturers)**



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## Assumptions

1. There is an accepted measure of **'benefit'** that patients derive from health care
2. **Funding new technologies** has an **opportunity cost** in terms of **foregone 'benefit'**
3. New technologies are **costly** to produce, and manufacturers will **not supply at a loss**
4. A **single threshold**, λ, is **publicly specified** by a health care system decision maker, with **new technologies adopted only if the ICER is less than λ**
5. Manufacturers of new technologies are **protected from price competition** (e.g. through the **patent system**), allowing for **super-normal profits**
6. Each adopted new technology is **strategically priced** such that the **ICER is equal to λ**
7. **Distributions** of **'reserve prices'** and **'reserve ICERs'** are **broad and continuous**
8. All 'reserve ICERs' are **non-negative** (technologies do not 'dominate' at 'reserve price')
9. Each new technology is **independent** and **developed by a different manufacturer**



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# Consumer perspective

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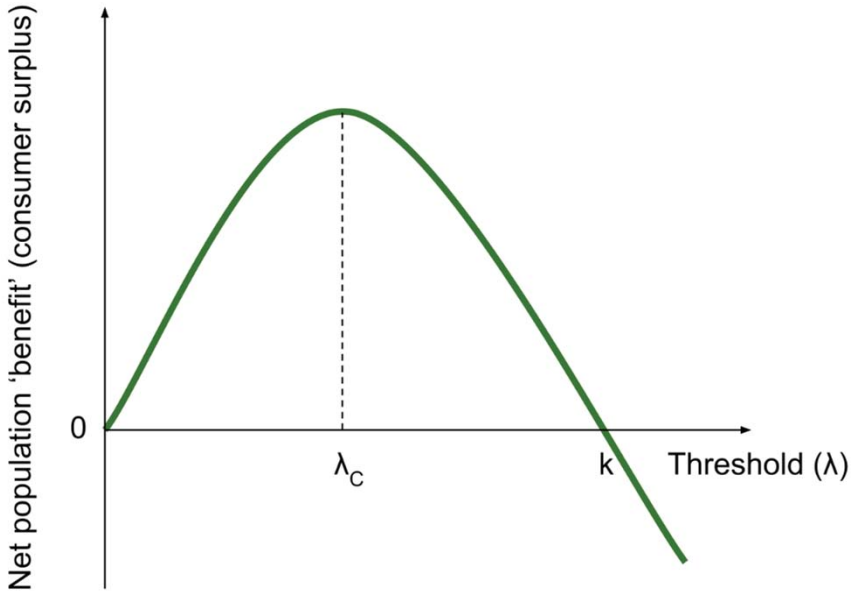




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# Producer perspective

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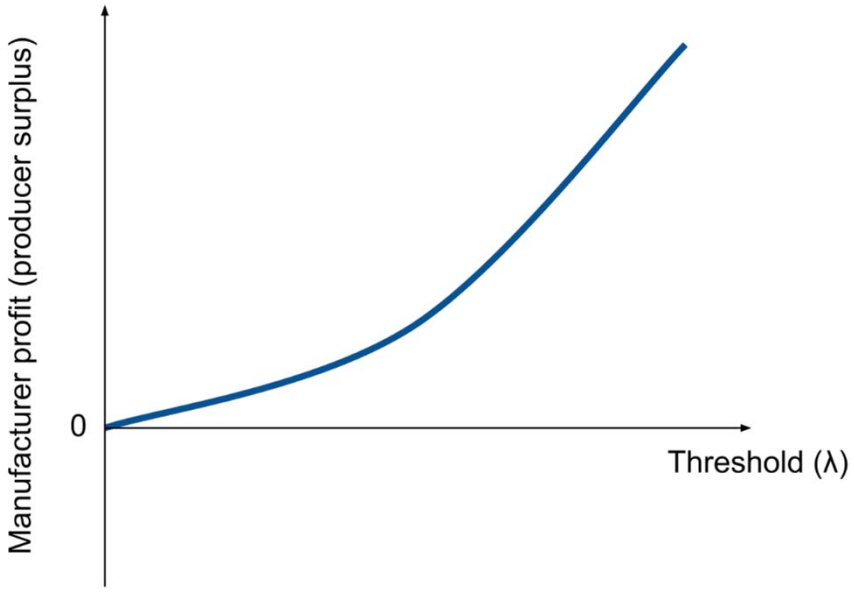




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# Combining the perspectives

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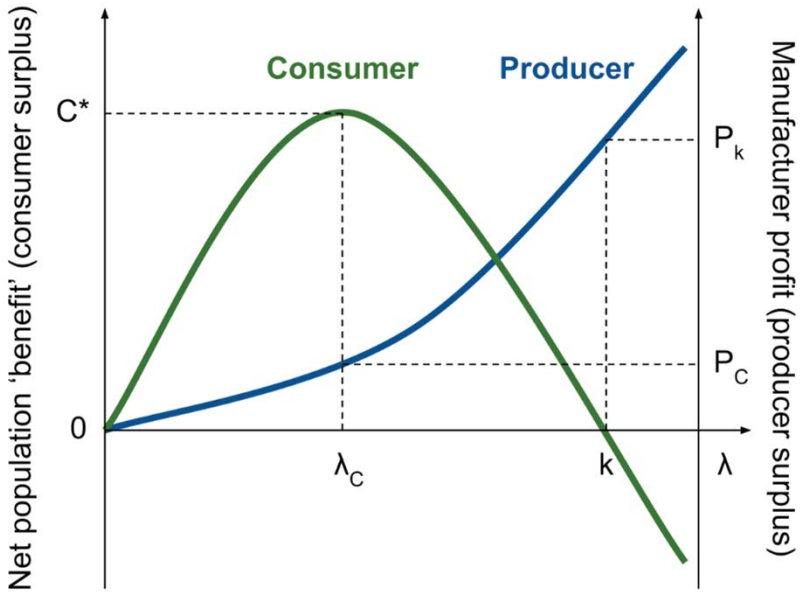
## Converting into a common metric

- Unless the measure of 'benefit' considered under the consumer perspective is already specified in **monetary terms**, combining consumer and producer surplus requires that each be considered using a **common metric**
- Whether this is done by converting consumer surplus into monetary terms or by converting producer surplus into units of 'benefit' is immaterial; the challenge is **identifying an appropriate conversion rate**
- A conventional **demand-side threshold** provides a natural source for such a conversion rate, since it provides an estimate of the **monetary value of a unit of 'benefit'** that **reflects society's preferences** (denoted as **v**)





# Policy objectives

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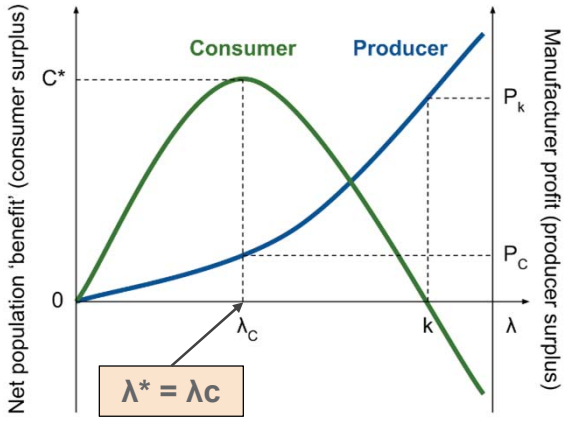
# ‘Maximize consumer surplus’




Consumer surplus is maximized by **specifying a threshold of λc**.

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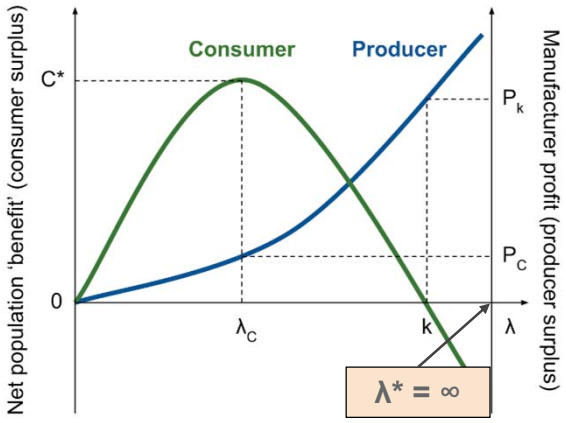
# ‘Maximize producer surplus’




Producer surplus is maximized with an **infinitely high threshold**.

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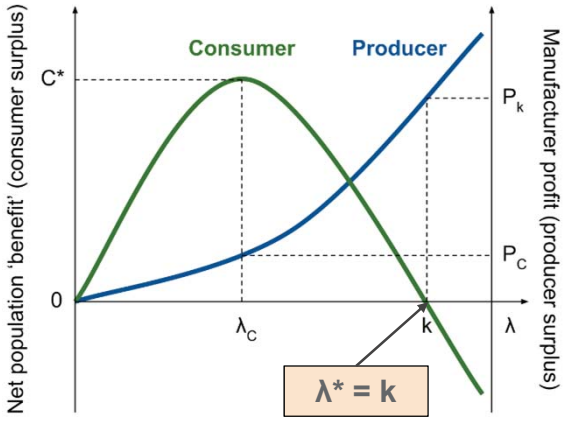
# ‘Max producer surplus, subject to consumer and producer surplus each being non-negative’




Since producer surplus increases with the threshold, and consumer surplus is negative at any threshold above **k**, this objective is satisfied by specifying a threshold of **k**.

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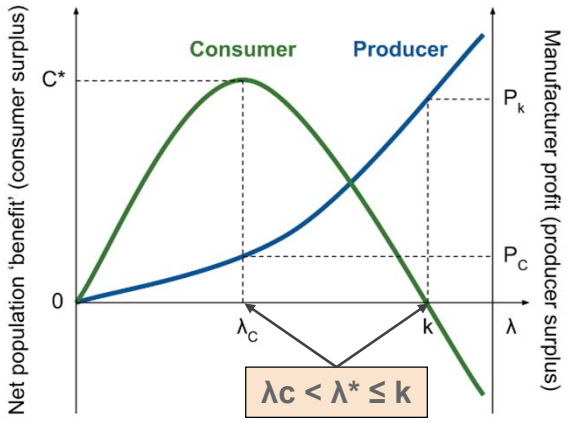
‘Maximize the combined surplus, subject to each being non-negative’




Since consumer and producer surplus both increase with the threshold up to **λc**, but consumer surplus is negative above **k**, the optimal threshold must lie between **λc** and **k**.

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# Conclusions

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## Implications for policy, theory, and empirical research

– – –

- The **optimal threshold** depends critically upon the **policy objective**
- Depending on the objective, the optimal threshold may be **lower** or **higher** than **either conventional approach** (supply-side or demand-side)
- A **supply-side** estimate of the threshold (k) is necessary to understand the shape of the **consumer threshold curve** and the **optimal threshold 'range'**
- A **demand-side** estimate of the threshold (v) is necessary to **convert consumer and producer surplus into a common metric**
- Future **empirical research** must estimate **not only k and v,** but also the **shapes of the consumer and producer threshold curves**



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Download slides from
https://goo.gl/Mv66HD
or by scanning barcode

## Any questions?



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# Appendix 2.4: Slides from 12 October 2018 (Dr Christopher McCabe)

# Supply side cost effectiveness thresholds for setting a ceiling price: some tools for unpacking the issues

Christopher McCabe PhD
University of Alberta
&
Institute of Health Economics

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## Decision problem

A new drug has been licensed that is expected to improve the health of recipients by two Quality Adjusted Life Years compared to current best practice.

What should the price regulator consider in arriving at a maximum price for this new drug?

1. Expected impact on population health
2. Expected impact on health system sustainability
3. Expected value of health = f(H.(d,p,t)
4. Reward to innovation = premium over cost of production of the innovation
5. Access to innovative treatments
6. Uncertainty

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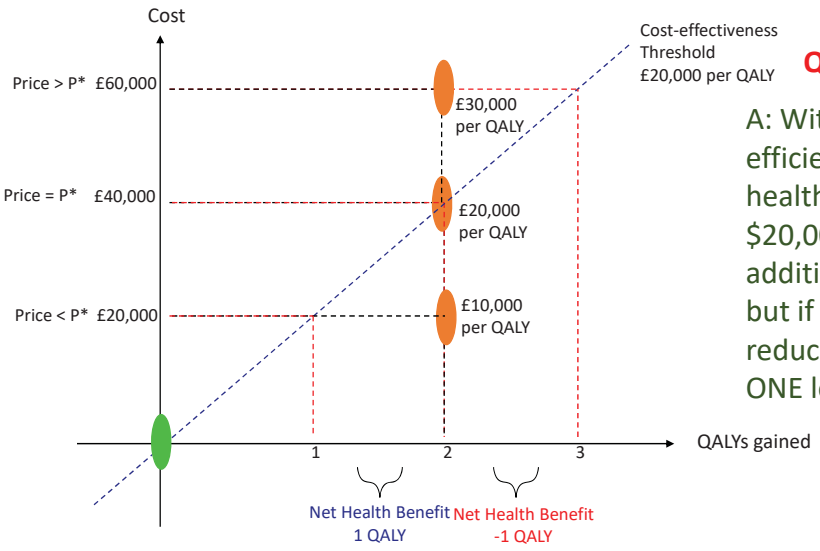
# Expected impact on health system sustainability




**Q: What does this mean?**

A: With its current budget and efficiency in producing health, if the health system budget was increased by $20,000 it would produce ONE additional Quality Adjusted Life Year; but if the health system budget was reduced by $20,000, it would produce ONE less Quality Adjusted Life Year.

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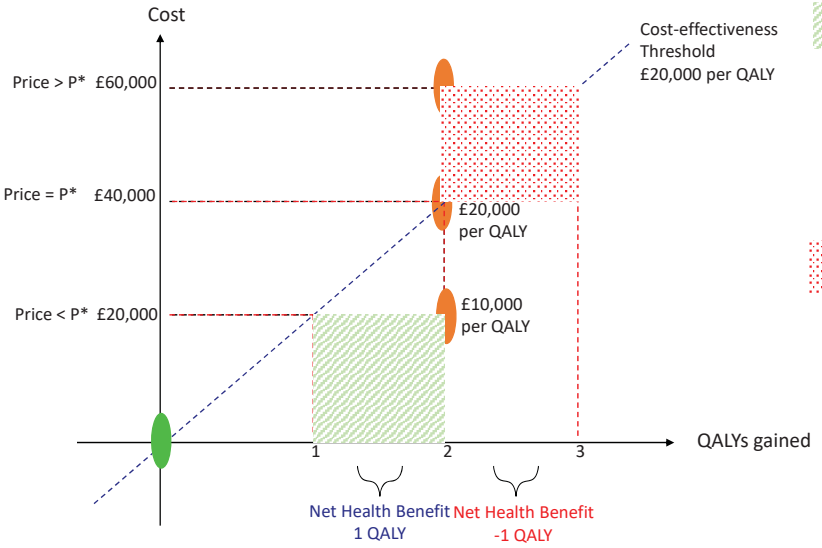
# Expected impact on health system sustainability




= Difference between the maximum health system would be willing to pay (give up) for the technology and what it actually has to give up = Consumer Surplus

+ve consumer surplus contributes to health system sustainability

-ve consumer surplus risks health system sustainability

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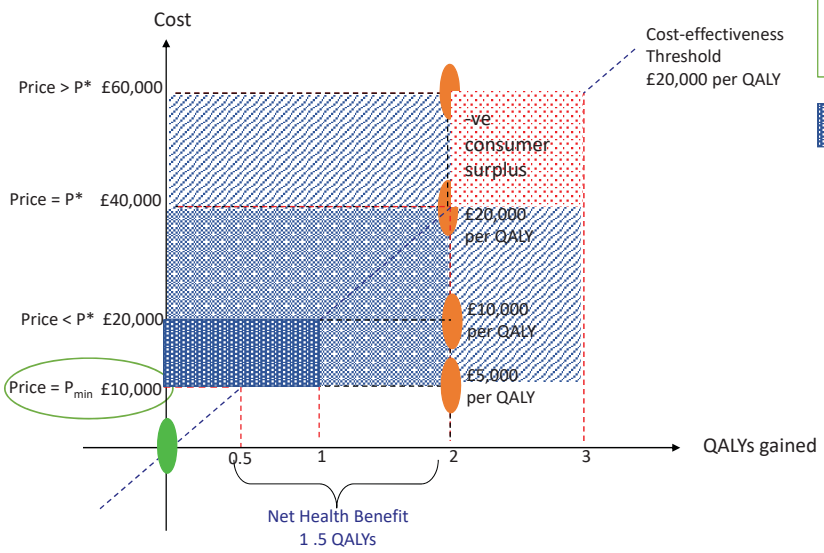
# Rewarding Innovation




$P_{min}$ = price which just covers the costs of production.

Price < $P_{min}$ = Drug will not be supplied to the market.

Difference between minimum price and the price received = Producer Surplus

Value of Innovation = Consumer Surplus plus Producer Surplus

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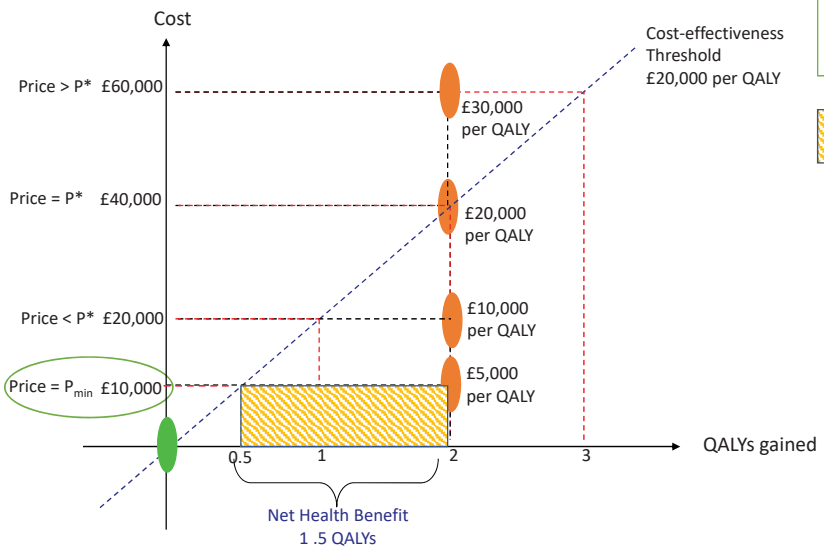
# Rewarding Innovation




$P_{min}$ = price which just covers the costs of production.

Price < $P_{min}$ = Drug will not be supplied to the market.

Welfare loss associated with drug not being supplied

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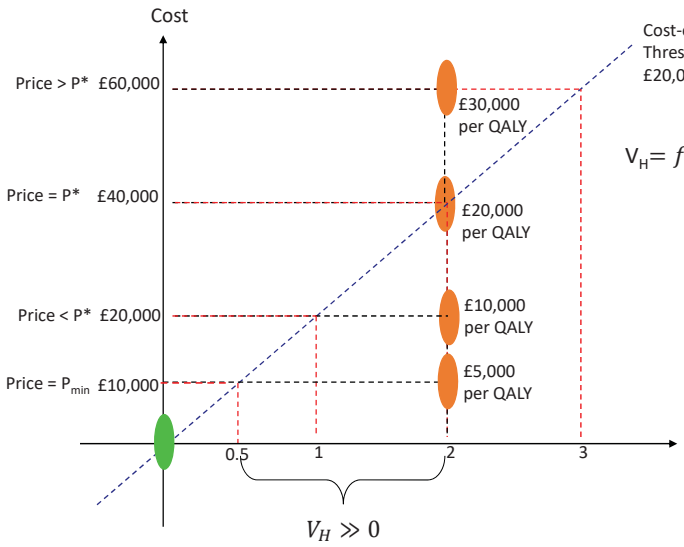
# Value of Health




$$V_H = f(H.(p,d,t))$$

Where:
$V_H$ = Value of Health
H = Health,
p = Vector of characteristics of population,
d = vector of characteristics of the disease

Pharmacoeconomics (2015) 33:255–269
DOI 10.1007/s40273-014-0234-z

ORIGINAL RESEARCH ARTICLE

**Value-Based Reimbursement Decisions for Orphan Drugs: A Scoping Review and Decision Framework**

Mike Paulden · Tania Stafinski · Davidas Menon · Christopher McCabe

Published online: 21 November 2014
© The Author(s) 2014. This article is published with open access at Springerlink.com

**Abstract**
*Background* The rate of development of new orphan drugs continues to grow. As a result, reimbursing orphan drugs on an exceptional basis is increasingly difficult to sustain from a health system perspective. An understanding of the value that societies attach to providing orphan drugs at the expense of other health technologies is now recognised as an important input to policy debates.
*Objectives* The aim of this work was to scope the social value arguments that have been advanced relating to the reimbursement of orphan drugs, and to locate these within a coherent decision-making framework to aid reimbursement decisions in the presence of limited healthcare resources.
*Methods* A scoping review of the peer reviewed and grey literature was undertaken, consisting of seven phases: (1) identifying the research question; (2) searching for relevant studies; (3) study selection; (4) charting, extracting and synthesising data; (5) analysing data; (6) consulting relevant experts; and (7) presenting results. The points within decision processes where the identified value arguments would be incorporated were then located. This mapping was used to construct a framework characterising the different ways in which societies value competing decision making.

Electronic supplementary material The online version of this article (doi:10.1007/s40273-014-0234-z) contains supplementary material, which is available to authorized users.

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**Key Points for Decision Makers**

Understanding the value that societies attach to reimbursing orphan drugs at the expense of other health technologies is important.

We have scoped the social value arguments advanced in the literature and located these within a coherent framework. This framework may be used to structure policy discussions and to aid transparency regarding the values underlying reimbursement decisions for orphan drugs in the presence of limited healthcare resources.

Decision makers should seek to identify which value-bearing factors they deem pertinent to their decision, whose preferences they wish to consider, and what value propositions underpin their decisions. These need to be consistently applied to all technologies and populations affected by the decision: the new orphan drug, any existing therapy for the same disease which will be displaced, and any therapies which will be displaced elsewhere in the system to fund any additional costs of a positive coverage decision.

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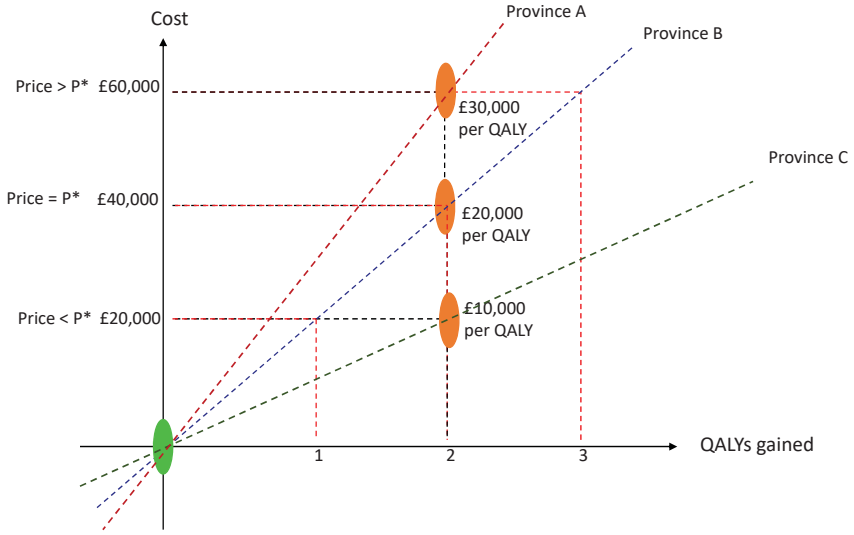
# Multiple budgets: multiple thresholds




Province A: P* Consumer Surplus = + 1/3 QALY or $10,000

Province B: P* Consumer Surplus = 0 QALYs

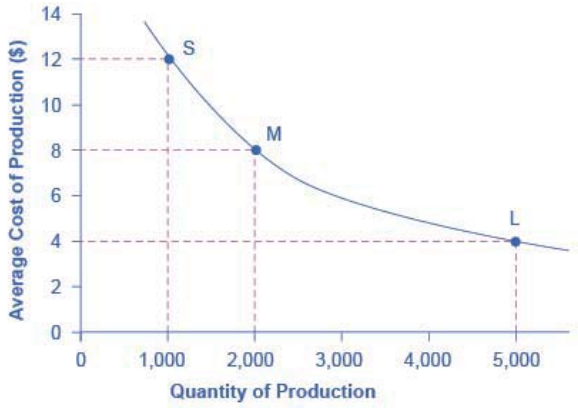
Province C: P* Consumer Surplus = -2 QALYs or -$20,000

P* Producer Surplus = $30,000

Social Welfare = (1/3*60,000) +0 + (-$20,000) = 0

8

# Unpacking market size: Market Size and Reserve Price ($P_{min}$)



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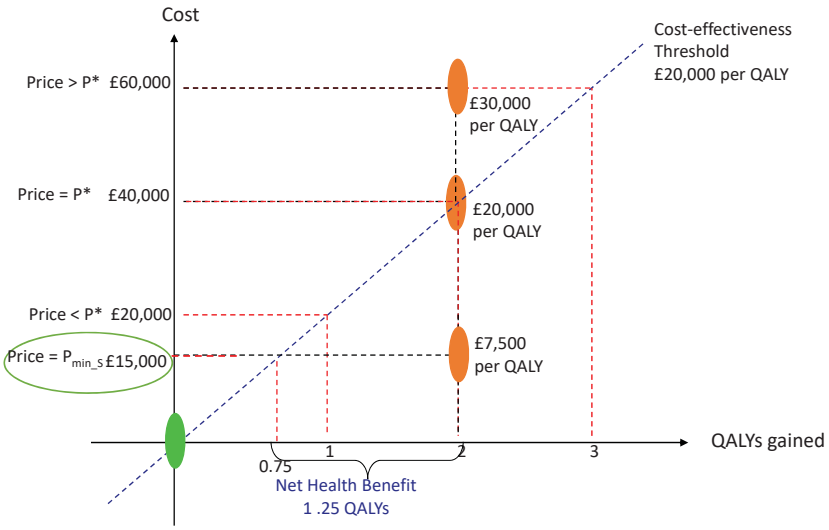
# Market Size and Reserve Price: Orphan

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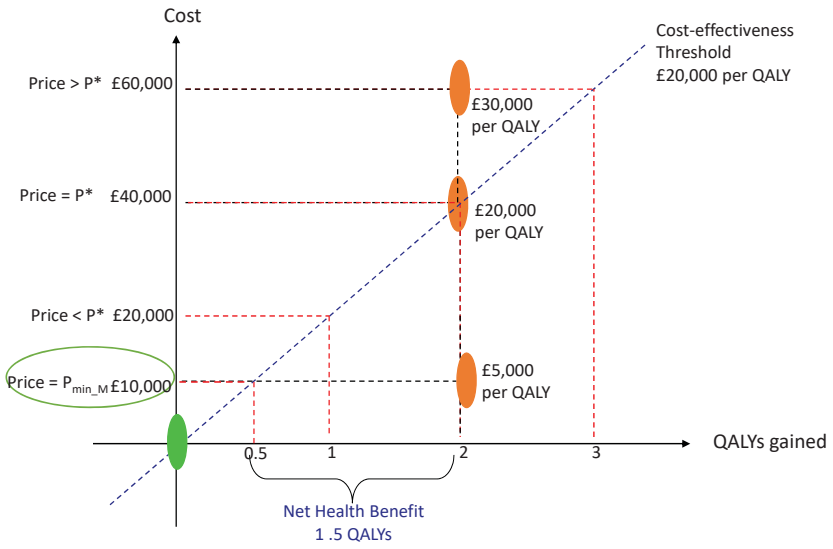
# Market Size and Reserve Price: Standard

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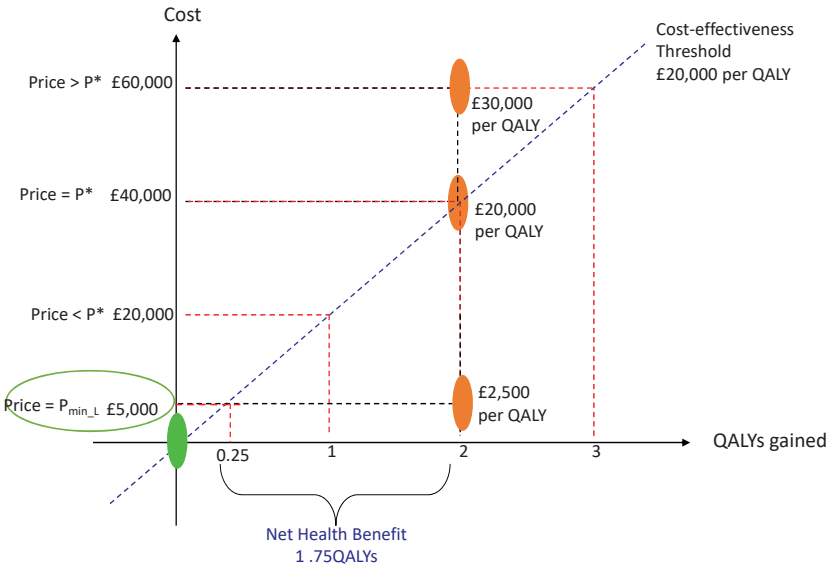
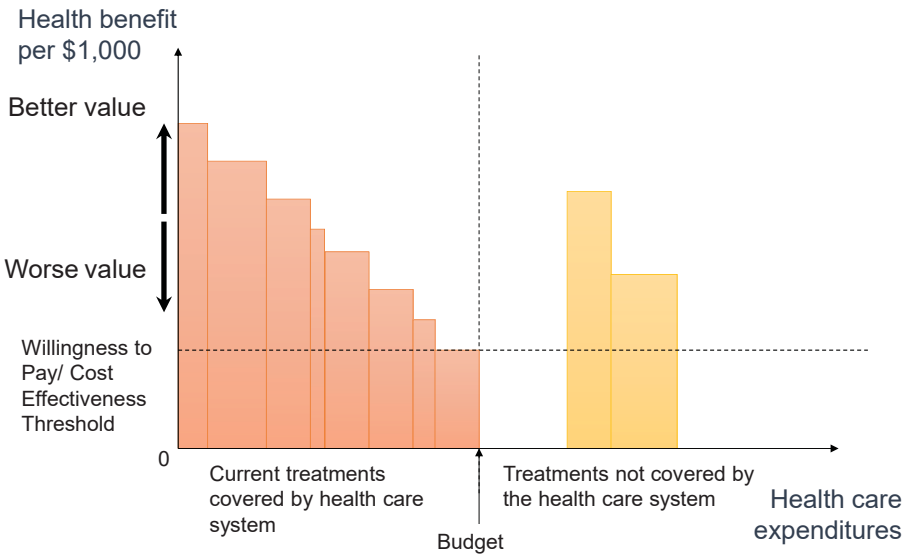
# Market Size and Reserve Price: Blockbuster




12

# Market size and budget impact

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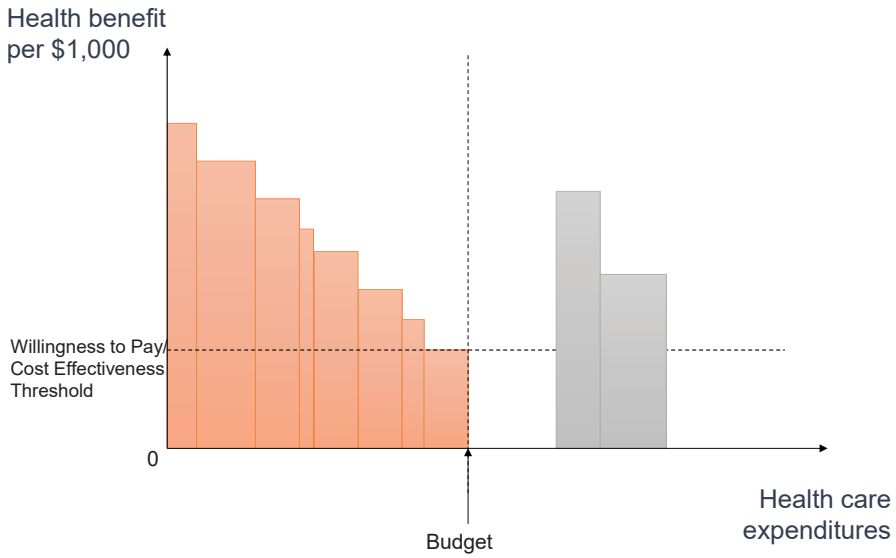
# Market size and budget impact

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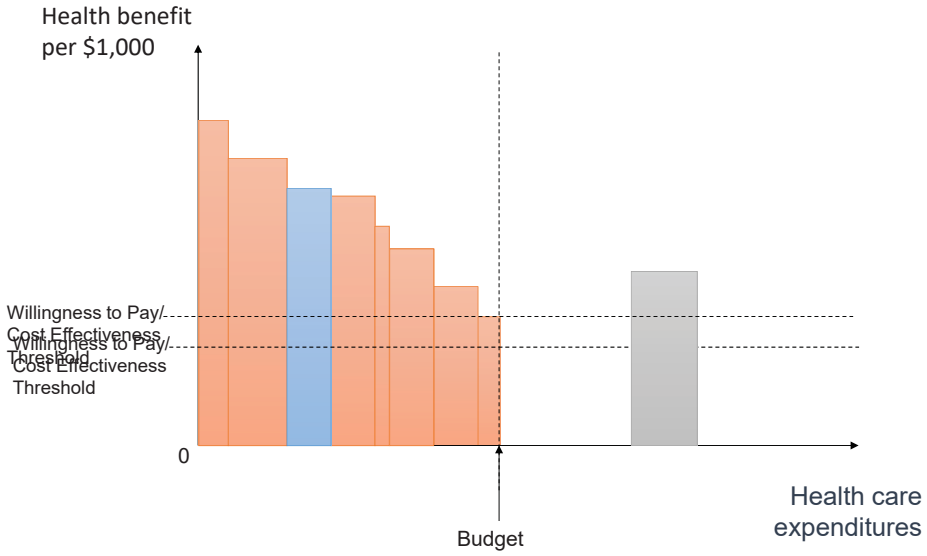
# Market size and budget impact

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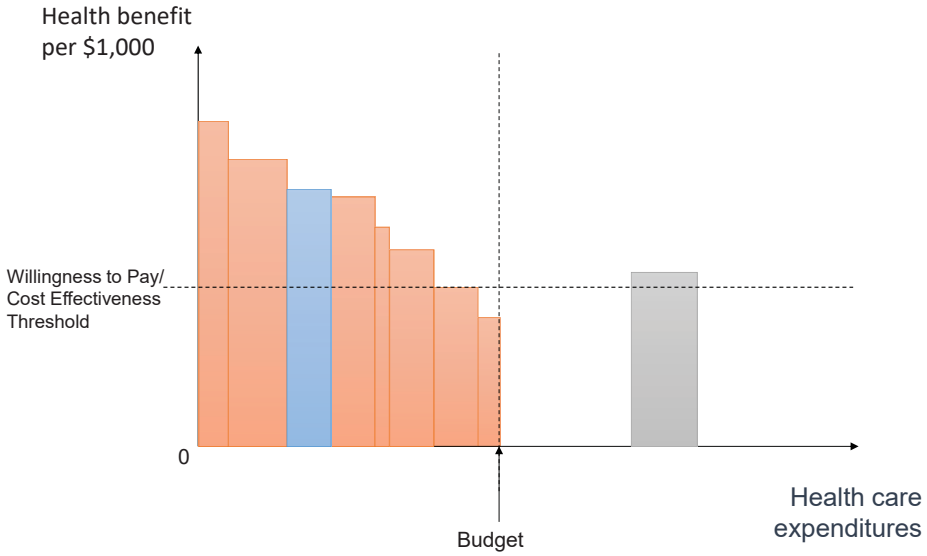
# Market size and budget impact

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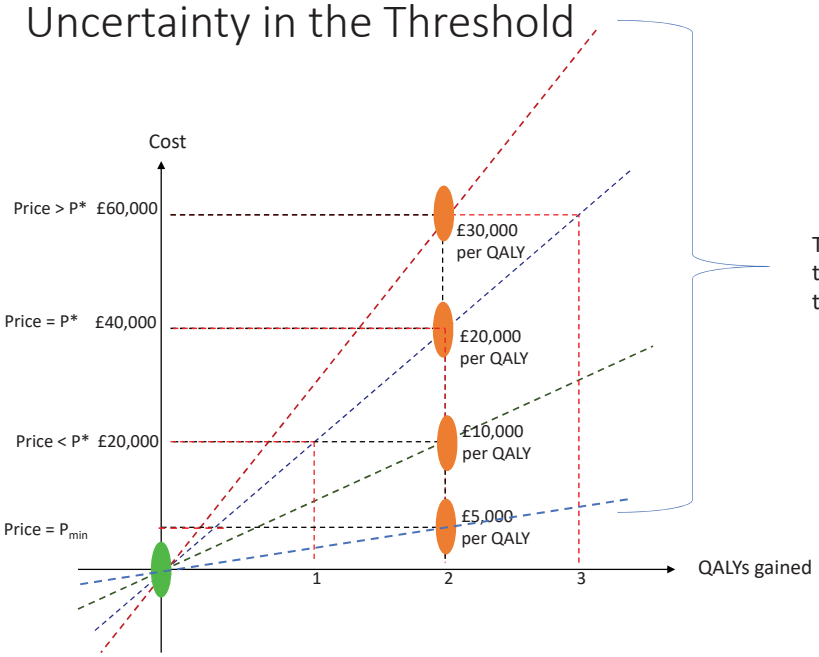
## Uncertainty in the Threshold

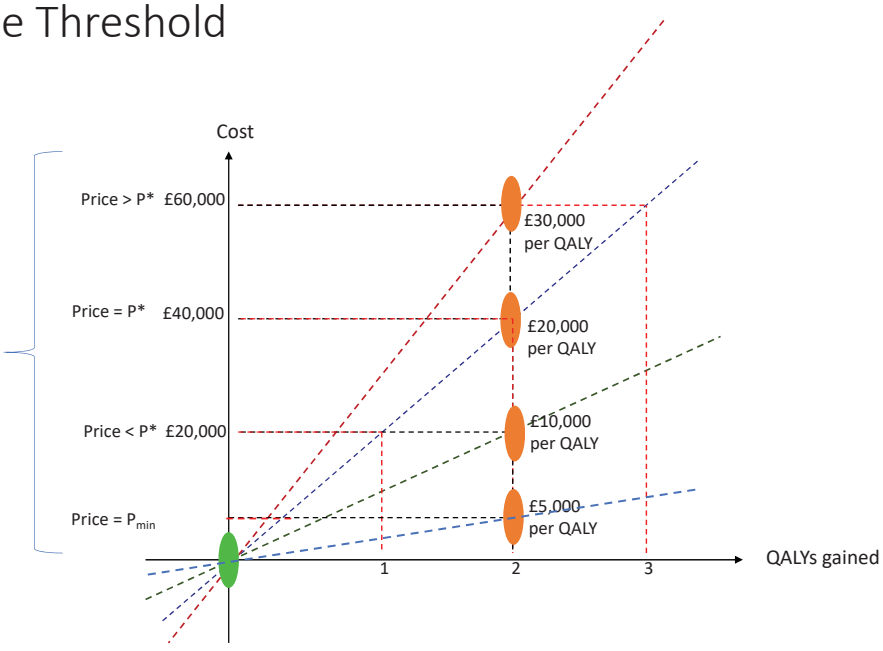



There is a probability that each of these thresholds is the 'true threshold

17

## Uncertainty in the Threshold

There is a probability that each of these prices is the actual minimum price.

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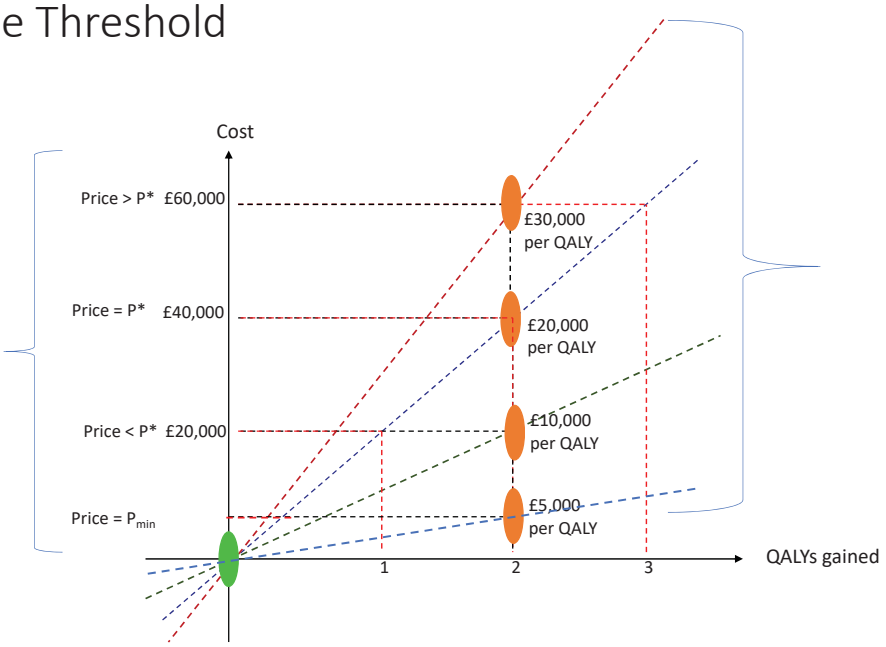
# Uncertainty in the Threshold

For any given ceiling price we can calculate and seek to minimise the expected value of the uncertainty (paying too much, paying too little, and losing access completely).




19

# Appendix 2.5: Slides from 5 February 2019 (Dr Mike Paulden)

*Note: The 'Draft Potential Recommendations' provided in these slides were discussed at the 5 February 2019 meeting. They were then revised, based on feedback from members, before a final set of 'Potential Recommendations' were voted on by the Working Group.*

# PMPRB Technical Working Group Meeting

5 February 2019

1

## Conceptual Framework

- The role of the Working Group was to examine and make recommendations to the Steering Committee regarding a number of specific technical issues. The Terms of Reference specified six distinct areas of focus for the Working Group to consider.
- This Conceptual Framework was drafted by the Chair prior to the final meeting of the Working Group. Its purpose was to guide the Working Group in making consistent recommendations across all six of these areas of focus, while respecting the policy intent and the range of views expressed by members of the Working Group throughout their deliberations.

2

## Economic principles

- At any given price, the 'economic surplus' from a good is the sum of two parts:
  - The 'consumer surplus', which is the benefit obtained by consumers because they are able to purchase the good at a price lower than their 'willingness-to-pay';
  - The 'producer surplus', which is the benefit obtained by producers because they are able to sell the good at a price higher than their 'willingness-to-accept'.
- In order to consider the consumer and producer surplus that might arise from the PMPRB setting a ceiling price on a new medicine, we must first specify demand and supply curves.

3

## Demand curve for a medicine

- The demand curve reflects society's willingness-to-pay for the medicine in question.
- It is for the PMPRB, rather than members of the Working Group, to define the components of this demand curve. The Working Group therefore defers to the government's policy intent when considering the relevant components of the demand curve.

4

## Policy intent

- During the Working Group's deliberations, the PMPRB stated that the most appropriate perspective to adopt is that of *Canada's publicly funded health care systems*.
- The 'Regulatory Impact Analysis Statement' (RIAS) (p.10) states that the *quality-adjusted life year (QALY)*, as used in cost-utility analysis, is regarded as the "gold standard" approach to considering the economic value of new medicines.
- In a July 2018 document prepared for the Working Group, the PMPRB clarified that the purpose of the PMPRB is to ensure that *patentees do not change excessive prices during the statutory monopoly period*.

5

## Demand curve for a medicine

- In light of this policy intent, a reasonable specification of the demand curve for a new medicine is based upon the net impact upon the health of patients (as measured in QALYs) associated with adopting the medicine within Canada's publicly funded health care systems for the duration of the statutory monopoly period.
- The net impact of a new medicine upon patient health is a function of two components:
  - The gain in health experienced by patients who receive the new medicine;
  - The loss in health experienced by other patients whose health care subsequently receives less funding than it would have done in the absence of the new medicine.

6

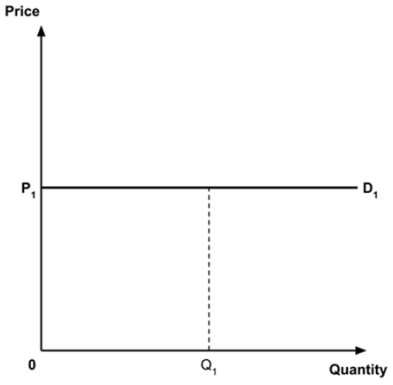
## Equity weighting

- Although the Terms of Reference required the Working Group to consider potential approaches for allowing higher ceiling prices for some medicines on the basis of specific characteristics (so-called 'equity weighting'), it was agreed by the Working Group that insufficient empirical evidence exists to do this at the present time. For the purposes of this conceptual framework, equity weighting is therefore not applied.

7

## Location of the demand curve

- The demand curve plots the ceiling price at which the incremental cost-effectiveness ratio (ICER) of the new medicine is equal to k

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## Supply curve for a medicine

- The supply curve plots the lowest price that a manufacturer would be willing to accept for a medicine. This is sometimes referred to as the 'reservation' (or 'reserve') price of the medicine.
- The supply curve is a function of a number of potential considerations, including the initial costs associated with developing the medicine, the marginal costs of production, and the potential implications for pricing in other jurisdictions as a result of 'reference pricing'.

9

## Supply curve for a medicine

- The components of the supply curve are complex.
- For the purposes of this framework, the medicine's supply curve will therefore be treated as unknown (and plotted as a dashed line).
- Despite being unknown, we may reasonably expect the supply curve for a medicine to have the following basic properties:
  - A relatively high intercept on the vertical axis, reflecting substantial initial costs associated with developing the medicine;
  - A downwards slope, reflecting a declining per-patient cost of supplying the medicine as the quantity supplied increases. This declining per-patient cost arises from the ability to spread the initial costs of development across a greater number of patients, and also potential economies of scale in the production of the medicine.

10

## Supply curve for a medicine


11

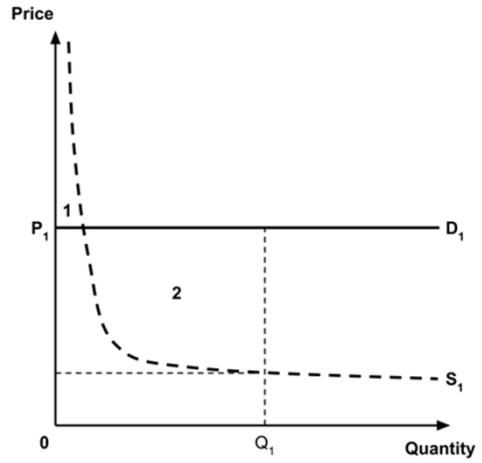
## Economic surplus

- The economic surplus is illustrated by the area of the region below the demand curve and above the supply curve, minus any area above the demand curve but below the supply curve, and bounded between the vertical axis and the quantity of medicine adopted.



12

## 1. Producer receives entire surplus (P1)

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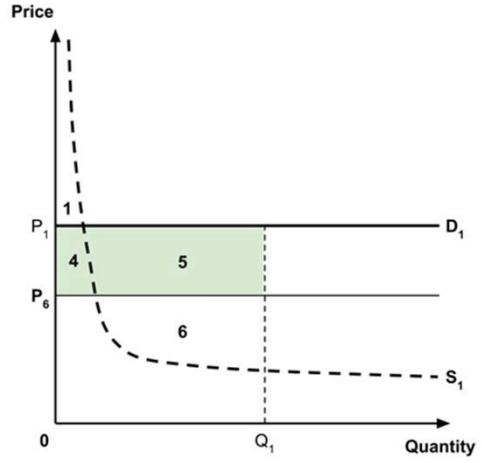
## 2. Consumers receive entire surplus (P6)

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# Topic 1: Options for determining what medicines fall into 'Category 1'

- A Category 1 medicine is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing.
- The following criteria have been identified as supporting a Category 1 classification:
  a) The medicine is 'first in class' or a 'substantial' improvement over existing options
  b) The medicine's opportunity cost exceeds its expected health gain
  c) The medicine is expected to have a high market impact
  d) The medicine has a high average annual treatment cost
- Should other criteria be considered? What are the relevant metrics for selecting medicines that meet the identified criteria and what options exist for using these metrics?

15

# Topic 1: Summary of Deliberations

- Should other criteria be considered?
  - No additional criteria were suggested by members of the Working Group.
- What are the relevant metrics and what options exist for their use?
  - Criterion B is impractical to implement as a screen.
  - Criterion D should be 'incremental' upon existing treatment.
  - Definitions should reflect practice elsewhere, ideally based upon existing definitions.
  - 'Thresholds' should be clearly specified, to provide a 'clear bright line' for manufacturers.
  - Metrics should result in a manageable number of Category 1 medicines for the PMPRB.

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## Topic 1: Draft Potential Recommendations

1. **The PMPRB should not consider any additional criteria.**
2. **The PMPRB should remove Criterion B from consideration.**
3. **Criterion D should be 'incremental' upon existing treatment.**
4. **Metrics for criteria A, C and D should reflect existing Canadian practice (e.g. based on existing definitions of 'substantial' treatment benefit).**
5. **'Thresholds' for each criterion should be determined by the PMPRB, taking into account the capacity for assessing Category 1 medicines, the technical considerations of the Working Group, and the policy intent.**
6. **'Thresholds' for each criterion should be clearly specified, so as to provide a 'clear bright line' to manufacturers.**

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## Topic 2: Application of supply-side cost effectiveness thresholds in setting ceiling prices

- Potential approaches for implementing a price ceiling based on a medicine's opportunity cost.
- Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc)

18

# Topic 2: Summary of Deliberations (1/2)

- Potential approaches for implementing a price ceiling based on a medicine's opportunity cost
  - An estimate of the 'supply-side cost-effectiveness threshold' ('k') allows for estimation of the health opportunity cost, in terms of forgone QALYs, associated with new medicines.
  - Conceptually, the Working Group expects 'k' to vary across provinces and territories.
  - The only estimate of 'k' currently available for Canada is that by Ochalek et al. (2018), which estimated 'k' to be $30,000 per QALY for Canada as a whole.
  - Concerns were raised about the instrumental variables (IVs) used for in this empirical work, and also the reliance upon UK (rather than Canadian) data.
  - Nevertheless, the $30,000 per QALY estimate of 'k' by Ochalek et al. (2018) is in the same ballpark as recent empirical estimates of 'k' published in other PMPRB12 countries (UK: £12,936 per QALY, Australia: $28,033 AUD per QALY, Spain: €24,870 per QALY).
  - Further empirical research is required to estimate 'k' in Canada - this should use Canadian data, appropriate IVs, and consider variation in 'k' across provinces/territories.
  - Any measure of opportunity cost used for setting a price ceiling should be clearly specified, so as to provide a 'clear bright line' for manufacturers.

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# Topic 2: Summary of Deliberations (2/2)

- Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc)
  - There is insufficient empirical evidence to implement 'equity weights' at the present time (as would be required to allow price ceilings above opportunity cost for some medicines).
  - There are technical considerations in implementing 'equity weights' in practice, including the need to respect horizontal equity by applying equity weights to all patients affected.
  - Applying equity weights to patients who bear the opportunity cost of new medicines requires an understanding of their characteristics, in addition to an estimate of the magnitude of health forgone (such that an estimate of 'k' is necessary but insufficient).
  - The PMPRB should support future empirical research in this area - this should estimate how 'demand side' willingness-to-pay for a QALY in Canada differs according to the characteristics of the patient, disease and/or technology in question.

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# Topic 2: Conceptual Framework

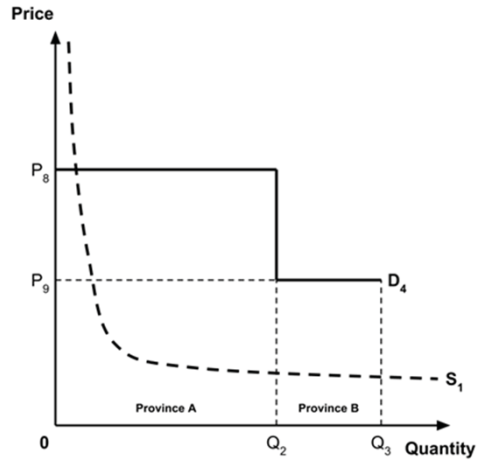
21

# Pricing across provinces and territories

- Since provinces and territories in Canada have some autonomy in setting health care budgets and prioritizing spending, it follows that $k$ would be expected to vary by province and territory.
- Since the demand curve plots the ceiling price at which the incremental cost-effectiveness ratio (ICER) of the new medicine is equal to k, it follows that the demand curve will be higher in provinces and territories with larger estimates of k.

22

## Pricing across provinces and territories




23

## Approaches for setting a single ceiling price

- The Working Group considered several approaches for setting a single ceiling price across provinces and territories, including:
  1. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the highest $k$ (such that the ICER equals this highest $k$);
  2. A ceiling price at which the medicine is 'just' cost-effective in the province or territory with the lowest $k$ (such that the ICER equals this lowest $k$);
  3. A ceiling price at which the medicine is 'just' cost-effective across Canada as a whole (such that the ICER equals a 'weighted average' of $k$ across Canada).

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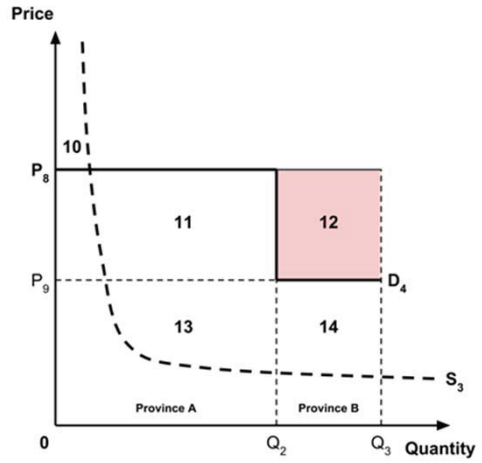
## Approach 1: Highest k

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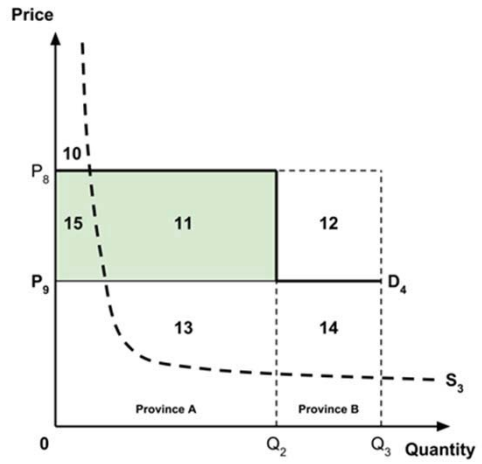
## Approach 2: Lowest k

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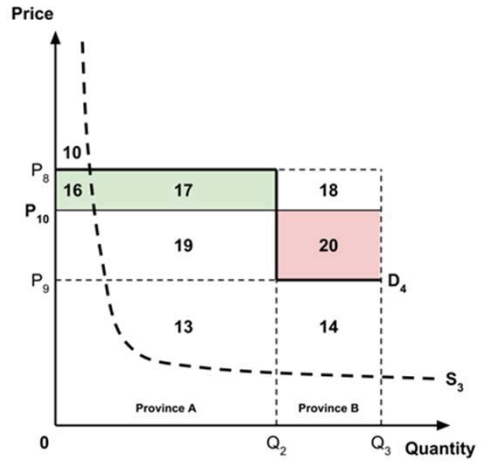
## Approach 3: Weighted average k




27

## Policy implications

- The most desirable approach for setting a single ceiling price across Canada depends upon the government's policy intent.
- *Note that it is not the role of the Working Group to specify the government's policy intent. While the implications of some potential policy objectives are considered below, this should not be construed as an endorsement by the Working Group of any particular policy objective. Also note that this analysis is not exhaustive: there are other potential policy objectives and approaches for setting a ceiling price across provinces and territories.*

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## Objective 1: No health loss across Canada

- The first approach is inconsistent with this policy objective. This is because this approach results in diminished population health (negative consumer surplus) in all provinces and territories except that with the highest k (in which consumer surplus is zero), resulting in diminished population health (negative consumer surplus) overall.
- The second approach comfortably satisfies this policy objective (since it results in positive overall consumer surplus), while the third approach only just satisfies this policy objective (since it results in an overall consumer surplus of zero).

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## Objective 2: No health loss in any province

- Both the first and third approaches are inconsistent with this policy objective. This is because both approaches result in diminished population health (negative consumer surplus) in at least one province or territory.
- The second approach would only just satisfy this policy objective, since consumer surplus is zero in the province or territory with the lowest $k$.

30

## Objective 3: Max health gain across Canada

- Consideration should be given to the location of the supply curve.
- Since the location of the supply curve is uncertain, this is challenging.
- Key assumption: a medicine will not be launched if producer surplus is negative.
  - If a medicine is not launched, the pharmacoeconomic value is zero since there is no resulting net gain in QALYs.
  - For the pharmacoeconomic value to be positive, the medicine must be launched at a ceiling price that results in positive consumer surplus.
- *The mandate of the PMPRB is to protect consumers from excessive pricing, not to ensure that products are launched into the market.*

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## Objective 3: Max health gain across Canada

- If the supply curve is understood to be sufficiently low that the medicine would be profitable at the ceiling price arising under the second approach (P9), then maximizing population health requires setting a ceiling price below P9, so as to maximize consumer surplus subject to producer surplus being non-negative.
- However, since the true location of the supply curve is uncertain, any reduction in the ceiling price carries a risk that producer surplus might become negative, such that the medicine would not launch at all. In such circumstances, consumer surplus would be zero, whereas at a higher ceiling price of P9 the new medicine would have launched and consumer surplus would have been positive.

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## Topic 2: Draft Potential Recommendations

1. **The Working Group regards the current evidence base with respect to the opportunity cost of adopting new medicines within Canada's public health care systems as highly uncertain. The PMPRB should be aware of limitations with the empirical work by Ochalek et al. (2018), including the reliance on UK data and the choice of instrumental variables (IVs) used. However, the direction of any resulting bias is unknown. Furthermore, the authors' $30,000 per QALY estimate of 'k' is in line with published empirical estimates of 'k' for other PMPRB12 countries.**
2. **The PMPRB should support further empirical research to estimate a 'supply-side cost-effectiveness threshold' ('k') for Canada. This research should consider and report on potential variation in 'k' across provinces and territories.**
3. **There is insufficient empirical evidence to implement 'equity weights' at the present time, as would be required to allow price ceilings above opportunity cost for some medicines but not others.**
4. **Any determinants of the price ceiling should be clearly specified, so as to provide a 'clear bright line' to manufacturers.**

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## Topic 3: Medicines with multiple indications

- Options for addressing medicines with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).

34

## Topic 3: Summary of Deliberations

- Indication-specific pricing is desirable in principle, since it would allow the price of each medicine to more closely reflect the medicine's value to patients in each indication.
- However, other countries which have implemented indication-specific pricing have a sophisticated IT infrastructure to support this, which Canada lacks.
- As a result, it is not feasible to implement indication-specific pricing in Canada at the present time.
- Rebenching of prices over time causes instability and uncertainty for manufacturers.
- Since manufacturers may choose the order in which indications are launched, and may avoid launching in specific indications altogether, any approach to pricing across indications may give rise to concerns of 'gaming' by manufacturers.

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## Topic 3: Conceptual Framework

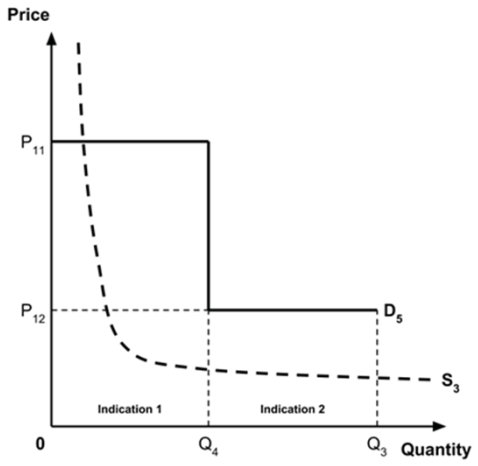
36

## Pricing across indications

- Where a medicine is available for multiple indications, this has implications for specification of the demand curve for a new medicine.
- If the per-patient health gain from the new medicine is different in each indication, then the ceiling price at which the ICER is equal to $k$ will also differ across indications.
- It follows that the demand curve will generally be different for each indication, with a relatively higher ceiling price corresponding to an ICER of $k$ for those indications in which the medicine has a relatively greater per-patient health gain.

37

## Pricing across indications



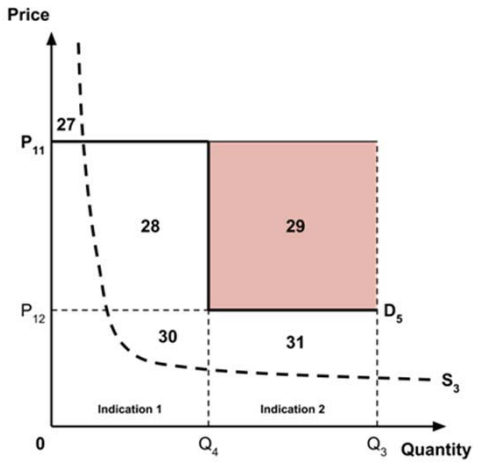

38

# Approaches for setting a single ceiling price

- The Working Group therefore considered various approaches for setting a single ceiling price across multiple indications, including:
  1. A ceiling price at which the medicine is 'just' cost-effective in the most cost-effective indication (such that the ICER equals $k$ in this indication);
  2. A ceiling price at which the medicine is 'just' cost-effective in the least cost-effective indication;
  3. A ceiling price at which the medicine is 'just' cost-effective across all indications (such that a 'weighted average' of the ICER across all indications equals $k$);
  4. A ceiling price at which the medicine is 'just' cost-effective in the first indication considered by the PMPRB (such that the ICER equals $k$ in this indication).

39

# Approach 1: Most cost-effective indication

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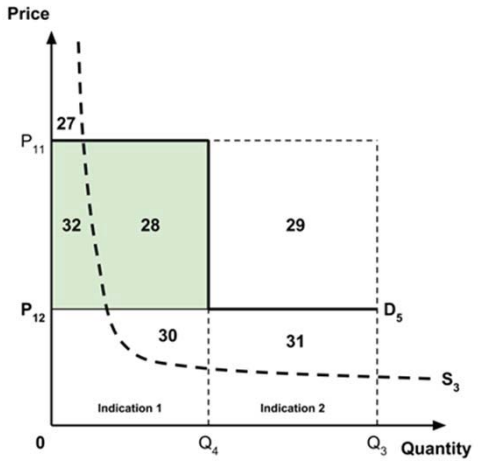
## Approach 2: Least cost-effective indication

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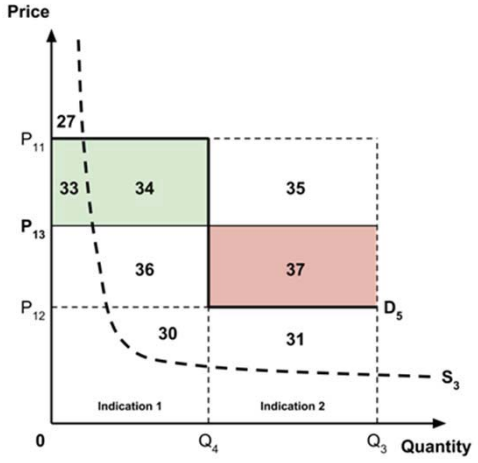
## Approach 3: 'Weighted average' of indications




42

## Approach 4: First indication considered

- This approach is the simplest to administer, since it does not require rebenching of ceiling prices in future if and when additional indications are launched.
- However, because producer surplus is unambiguously greater at a ceiling price of $P_{11}$ than $P_{12}$, this approach provides an incentive for the manufacturer to launch in the most cost-effective indication first to secure a higher ceiling price for future indications.

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## Approach 4: First indication considered

- If manufacturers act upon this incentive and are perfectly strategic, then this approach would have the same implications for consumer surplus as Approach 1.
- If manufacturers do *not* act upon this incentive, then in some cases consumer surplus from additional indications will be positive (if a less cost-effective indication is launched first) and in other cases consumer surplus from additional indications will be negative (if a more cost-effective indication is launched first). If the decision as to which indication to launch first is truly random, then a reasonable expectation would be that the *expected* consumer surplus associated with additional indications is zero. This would have equivalent implications for consumer surplus as Approach 3.
- It follows that this approach may be considered as lying somewhere between Approach 1 and Approach 3, with expected consumer surplus ranging between negative (if manufacturers are in any way strategic) to zero (if manufacturers are not strategic at all).

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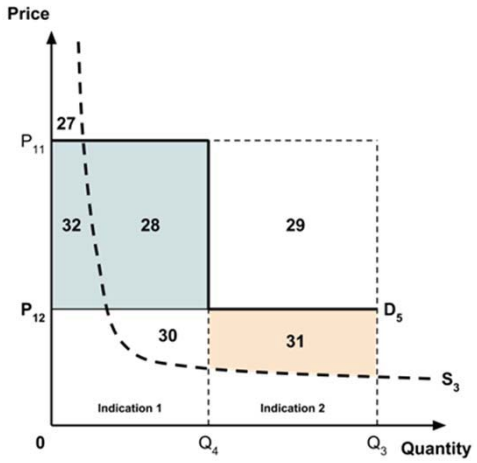
## Potential for strategic behaviour

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## Objective 1: No health loss across Canada

- The first approach is inconsistent with this policy objective
- The second approach comfortably satisfies this policy objective (since it results in positive overall consumer surplus)
- The third approach only just satisfies this policy objective (since it results in an overall consumer surplus of zero)
- The fourth approach satisfies this policy objective *if manufacturers are not strategic*, but if manufacturers behave strategically then the expectation would be that consumer surplus is negative overall, in which case this approach would *not* satisfy this objective.

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## Objective 2: No health loss in any indication

- Both the first and third approaches are inconsistent with this policy objective. This is because both approaches result in diminished population health (negative consumer surplus) in at least one indication.
- The second approach would only just satisfy this policy objective, since consumer surplus is zero in one indication and positive in all others.
- The fourth approach satisfies this policy objective *if manufacturers always launch in the least cost-effective indication first*, otherwise it does not satisfy this objective

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## Objective 3: Max health gain across Canada

- The most desirable ceiling price under this policy objective is the lowest ceiling price at which producer surplus is non-zero.
- Depending upon the location of the supply curve, this might be at a ceiling price below $P_{12}$, leading to greater consumer surplus than that resulting from any of the four approaches considered above.
- However, as before, lowering the ceiling price to extract additional consumer surplus carries a risk that producer surplus may become negative, such that the medicine is not launched and consumer surplus is zero.

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## Topic 3: Draft Potential Recommendations

1. **Since indication-specific pricing is not currently feasible, the PMPRB should specify a single ceiling price for each medicine that applies across all indications.**
2. **This ceiling price should be consistent with the government's policy intent with regards to the allocation of consumer and producer surplus.**
3. **The PMPRB should support efforts to develop the necessary infrastructure to allow for indication-specific pricing in future.**

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## Topic 4: Accounting for uncertainty

- Options for using the CADTH and/or INESS reference case analyses to set a ceiling price.
- Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.

50

## Topic 4: Summary of Deliberations

- Options for using the CADTH and/or INESSS reference case analyses to set a ceiling price
  - CADTH guidelines (4th edition) describes principle methods, but differences between the CADTH and INESSS reference cases, and between each analyst's consideration of uncertainty, may lead to different point estimates of the ICER
  - PMPRB could specify its own 'reference case', including a preferred 'threshold' & perspective
  - PMPRB could set up a committee to review the economic evidence
  - Price adjustments may be needed as real world evidence changes
- Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.
  - CADTH currently reports a range for the reference case ICER, not a point estimate
  - 'Price reduction tables' reported by CADTH not subject to peer review
  - CADTH methods (4th edition) mandate probabilistic analysis
  - Use the expected values or the upper/lower end of the range?

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## Topic 4: Conceptual Framework

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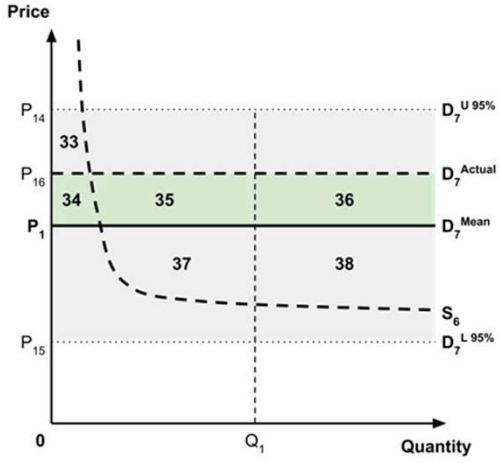
## Uncertainty


53

## Actual demand curve higher, drug launched

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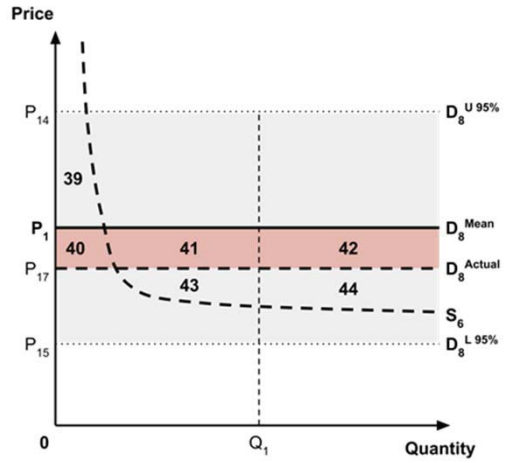
## Actual demand curve lower, drug launched

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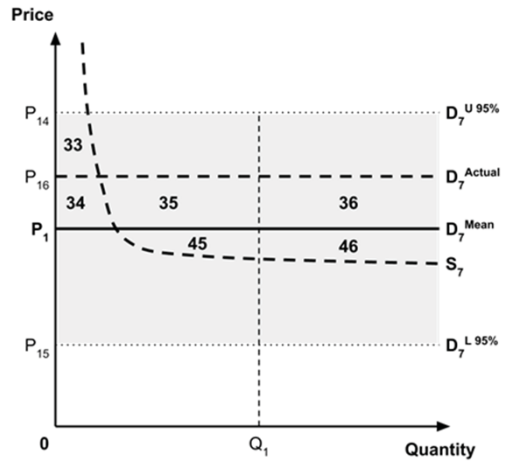
## Actual demand curve higher, not launched

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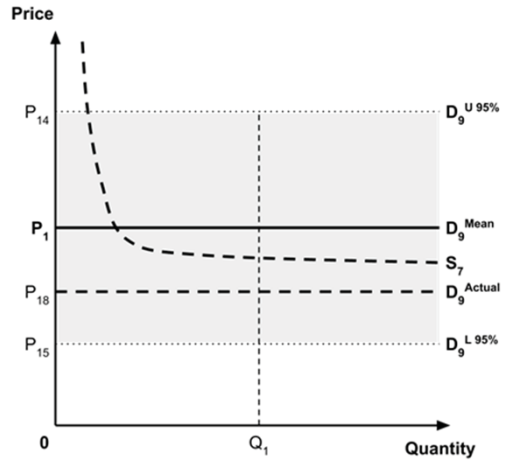
## Actual demand curve lower, not launched

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## Implications of uncertainty

- If the medicine is launched at a ceiling price coinciding with the expected demand curve then the expected consumer and producer surplus is zero.
- If the medicine is unprofitable at a ceiling price coinciding with the expected demand curve, and is also unprofitable at a ceiling price coinciding with the actual demand curve, then consumer surplus is zero.
- If the medicine is unprofitable at a ceiling price coinciding with the expected demand curve, but would have been profitable at a ceiling price coinciding with the actual demand curve, then the impact of uncertainty is to diminish the total economic surplus such that the impact upon expected consumer surplus at a ceiling price coinciding with the expected demand curve is negative.

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## Value of information analysis

- In conventional pharmacoeconomics, the expected loss that results from uncertainty is estimated using 'value of information' (VOI) analysis.
- Since the focus of conventional pharmacoeconomic analysis is making a yes/no decision regarding adoption of a new medicine, conventional VOI analysis considers the expected loss associated with making the 'wrong' decision (e.g. approving a medicine that would otherwise have been rejected, or *vice versa*).
- In the context of the PMPRB using 'pharmacoeconomic value' as a factor when considering the ceiling price for a new medicine, the expected loss as a result of uncertainty comes not from making the 'wrong' yes/no decision, but from setting the 'wrong' ceiling price.

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## Value of information analysis

- In principle, VOI analysis could be used to estimate this expected loss, and hence the value associated with obtaining additional sample information for one or more uncertain parameters. The results of these analyses could then be used to apply a reduction to the ceiling price of the medicine to reflect the diminished expected pharmacoeconomic value as a result of uncertainty.
- However, conducting such VOI analyses would require an understanding of the location of the supply curve, since this is required to estimate the expected loss in economic surplus, and in practice the location of the supply curve is unknown. Although, in principle, the supply curve could be modelled with a probability distribution in order to permit VOI analysis to take place, methods for estimating the parameters of such a distribution are undeveloped. It may therefore be infeasible to conduct VOI analyses of this type at the present time.

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## Topic 4: Draft Potential Recommendations

1. **The PMPRB should consider its attitude towards risk**
2. **If the PMPRB is risk-neutral, the *expected* values of the incremental costs and QALYs and k should be used when considering the ceiling price**
3. **If the PMPRB is *not* risk-neutral, values above or below the expected values may be appropriate, depending upon the risk attitude**
4. **The value of obtaining additional information for uncertain parameters should not be routinely considered by the PMPRB at the present time**

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## Topic 5: Perspective

- Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a 'significant' difference between price ceilings under each perspective.
- How to define a 'significant' difference in price ceilings between each perspective.

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## Topic 5: Summary of Deliberations

- **PMPRB intervened to state that public payer perspective is preferred**
- Prior to this, the Working Group considered how reforms have implications for private payers and individuals paying out of pocket
- A broad 'societal' perspective is problematic for reasons of principle (e.g. equity) and practicality (specifying productivity, spillover effects, caregiver burden, etc.)
- Concern that excluding productivity would impact private payers
- Cash paying customers will be excluded from the confidential MRP ceiling price
- Benefits to private payers might not be transferred back to end users

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## Topic 5: Draft Potential Recommendations

1. **Given the policy intent, the public payer perspective should be adopted**
2. **The PMPRB should be aware of the potential implications of its reforms for private payers and individuals**

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## Topic 6: Application of the market size factor in setting ceiling prices

- Approaches to derive an appropriate affordability adjustment to a medicine's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' approach).

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## Topic 6: Summary of Deliberations

- Different payers have different tolerances for expenditure growth
- In the UK, NICE recently agreed to cap expenditure growth on new medicines by 2% per annum
- Members considered the US ICER approach, which moved away from considering GDP factors when setting prices
- Market size is distinct from 'net budget impact'
- Particular implications for whether orphan drugs are profitable
- Market size not always known at launch (uncertainty)

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# Topic 4: Conceptual Framework

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## Market size

- The PMPRB has proposed that a 'market size adjustment' may be applied to the ceiling price for some Category 1 medicines. This includes a potential upwards ceiling price adjustment for medicines with small market size and (independently) a potential downwards ceiling price adjustment for medicines with large market size.
- The first of these would have the effect of increasing the producer surplus (at the expense of consumer surplus) for medicines with small market size. The second would increase the consumer surplus (at the expense of producer surplus) for medicines with large market size.

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## Without market size adjustment


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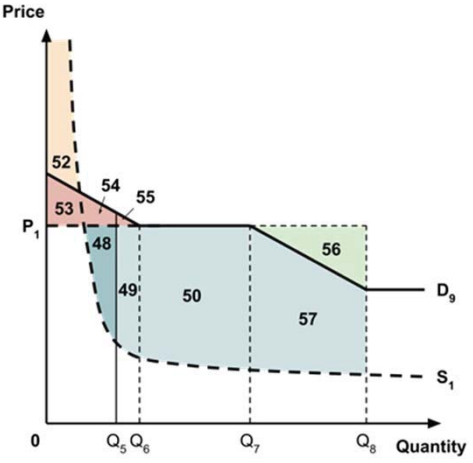
## With hypothetical market size adjustment

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## Implications of a market size adjustment

- Increased consumer surplus from medicines with large market size
  - The reduction in the ceiling price for medicines with large market size results in an increase in consumer surplus and a reduction in producer surplus
- Reduced consumer surplus from medicines with small market size
  - A higher ceiling price for medicines with small market size results in greater producer surplus and a loss in consumer surplus
  - Since (in this example) consumer surplus was zero prior to the market size adjustment, consumer surplus is now negative for medicines with small market size.
- Increased profitability for medicines with small market size
  - Medicines with a market size between Q5 and Q6, which were unprofitable prior to the market size adjustment, now have positive producer surplus.
  - This might result in greater access to medicines with small market size.

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## Potential risks and disincentives

- If the reduction in ceiling price for medicines with large market size is large, then manufacturers may be incentivized to reduce the quantity supplied so as to avoid the reduction in the ceiling price. This risk is particularly acute if the medicine in question has multiple indications, and if pricing across all indications is based upon the least cost-effective indication - as discussed earlier, this pricing approach might already provide an incentive for manufacturers to avoid launching in one or more indications, and the addition of a market size adjustment might exacerbate this risk.
- By providing a higher ceiling price for medicines with low market size, a market size adjustment would also relatively incentivize the development of such medicines. Over time, a reduction in medicines with large market size and an increase in medicines with small market size might result in progressively smaller gains and progressively larger losses in consumer surplus as a result of the market size adjustment.

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## Topic 6: Draft Potential Recommendations

1. **The PMPRB should ensure that any market size adjustment results in the MRP changing smoothly with the market size**
2. **The PMPRB should consider the implications for consumer and producer surplus, and ensure these are consistent with the policy intent.**
3. **The PMPRB should consider potential disincentives that might result from application of a market size adjustment**

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# Appendix 3: ‘On The Record’ Comments

# Appendix 3.1: Email from Frédéric Lavoie and Geoff Sprang (1/4)

*Subject: Working Group meeting of July 26, 2018*

*Date: 9 August 2018 at 15:21 MST*

*From: Frédéric Lavoie*
*To: Mike Paulden*
*Cc: Geoff Sprang*

Dear Mike,

On behalf of BIOTECanada and Innovative Medicines Canada, we would like to thank you for chairing the first face to face meeting of the PMPRB Working Group held on July 26, 2018. Although the industry associations we represent do not support the use of economic factors such as cost-effectiveness analyses as part of the proposed amendments to the Patented Medicines Regulations, and are also concerned about the initiation of Guidelines consultations before the finalization of regulatory changes, we felt that you were open to our points of view and invited us with the upmost respect to contribute throughout the meeting.

As the Working Group terms of reference stipulate that points of contention will be recorded by the Chair and reflected in the Working Group final report, we felt it would be appropriate to summarize our perspectives in writing and to provide you with our views on the discussions during the meeting.

**Observations on the discussions:**

We perceived during the meeting with the academic experts and other stakeholders represented at the Working Group that consensus cannot be achieved for the implementation of economic factors for the purpose of setting price ceilings for patented medicines in Canada. The debates that we observed around the table reinforced the apprehension our industry has communicated regarding the use of pharmacoeconomic factors, and made it clear that it is imperative for the Working Group to communicate to the Steering Committee and to the Federal Government the challenges presented by the proposed use of these factors, so that the scope of discussions with our industry and other stakeholders can be extended to include the consideration of alternative regulatory approaches as quickly as possible.

**Determination of a willingness to pay threshold and the use of pharmacoeconomic factors at the PMPRB level:**

When it comes to economic factors such as pharmacoeconomics, the proposed utilization of a threshold and of a cost-utility point estimate in the process involving Category One products (as first disclosed by the PMPRB to stakeholders on June 25th, 2018) would produce tremendous uncertainty and is therefore unacceptable.

The different schools of thought and academic debates around the establishment of a willingness to pay threshold through supply side or demand side methods are diverse and evolving. Even if an academic consensus were achievable, the implantation of a single method would always lead to a point estimate around which a distribution of possible results would reflect the high degree of uncertainty that exists regarding the establishment of a willingness to pay threshold and its variability across the diversity of Canadian perspectives it needs to reflect. Citing the work of Neumann et al. on this topic reflects this point: ”Searching for a single benchmark is at best a quixotic exercise because there is no threshold that is appropriate in all decision contexts.” (N ENGL J MED 371;9, August 28, 2014).

The same issue arises from the assessment of cost utility where substantial variability exists around the numerator and the denominator of the cost utility ratio compounded by the variability observed as a function of the analyst that produces the assessment and the peer reviewers that challenge the analyses (i.e. industry, CADTH, INESSS, the private sector, etc.). A review of recent CADTH CDR and pCODR recommendations conducted by Innovative Medicines Canada and EY shows that the degree of divergence between the cost-utility thresholds produced by CADTH versus those submitted by industry is significant: ICURs based on CADTH reassessment are significantly higher than those submitted by the manufacturers in the majority of cases; with the difference being as high as two to three times in many cases. The distribution of possible results around these point estimates is invariably wide and it is therefore inappropriate as a metric for setting the price ceilings of patented medicines. In addition, the perspective employed in CADTH CDR or pCODR submissions is a public drug plan perspective in accordance with the guidance provided by CADTH, and it is inappropriate to apply these pharmacoeconomic analyses to the entire Canadian population.

Given these significant limitations, it is inadvisable to use such an imprecise test of cost utility, compared against an equally controversial willingness to pay threshold, to determine a price ceiling for an innovative medicine. Its usage will lead to frequent and potentially litigious disputes requiring human and financial resources that are best deployed elsewhere by both the regulator and the regulated.

Furthermore, as many of our member companies operate on a global scale and have limited resources to allocate to meet the significant tasks required to bring a product to any individual market around the world, the regulatory signals sent by individual countries need to be as clear as possible to incentivize companies to launch innovative medicines. Contrary to the stated

objective of PMPRB's proposed new framework, the proposed set of economic factors will provide no "bright line" that will "yield ceiling prices that are foreseeable to patentees". Under such uncertain circumstances, it is foreseeable that many companies will delay or even forgo the launching of new innovative medicines in Canada.

**Risk categorization:**

The categorization exercise proposed by the PMPRB is only notionally consistent with the industry's proposal for a risk-based approach to pricing regulatory scrutiny. As was evident from the Working Group discussions, the identification application of specific criteria must be the subject of careful consideration to avoid unintended consequences. If the categorization is too broadly defined, as was the case with the initial information disclosed by PMPRB to stakeholders on June 25th, 2018, the number of patented medicines that will be subject to an elevated level of regulatory scrutiny will be too large. This in turn will impose a significant operational burden on both the regulator and the regulated, while failing to achieve the stated policy objective of focussing regulatory resources where they add the most value. Furthermore, this categorization needs to be correlated with the magnitude of the risks that concern policy makers. The PMPRB has not offered a compelling policy rationale for each of the proposed screening criteria. From the discussion at the Working Group, we believe that the potential impact of including these criteria requires further evaluation.

Once again, we thank you for listening to our perspective on behalf our industry associations, and for ensuring that the content of this communication is reflected in the proceedings of the Working Group and also communicated back to the Steering Committee.

We look forward to a continued constructive dialogue with you and the Working Group.

Frederic and Geoff

# Appendix 3.2: Email from Frédéric Lavoie and Geoff Sprang (2/4)

*Subject: Draft summary of 26 July Working Group meeting*

*Date: 17 August 2018 at 11:17 MST*

*From: Frédéric Lavoie*
*To: Mike Paulden, Chris Cameron, Christopher McCabe, Donald Husereau, Doug Coyle, Karen Lee, Maureen Smith, Patrick Dufort, Peter Jamieson, Stuart Peacock, Tammy Clifford, Tania Stafinski*
*Cc: Edward Burrows, Douglas Clark, Guillaume Couillard, Isabel Jaen Raasch, Matthew Kellison, Nelson Millar, Richard Lemay, Tanya Potashnik, Theresa Morrison, Geoff Sprang*

Dear Mike,

We wanted to draw your immediate attention to some issues regarding the minutes.

After we sent you by email on August 9, 2018 (attached for reference) a summary of our industry perspectives and our views on the discussions during the first meeting of the technical working group (TWG), we have become aware that meeting minutes from the first meeting of the TWG have been shared with the PMPRB Steering Committee in advance of those minutes being shared and validated with the working group members themselves. As the terms of reference of the TWG stipulates that “the chair shall have final say on all matters of governance and procedures” we feel important to request that certain governance processes be improved. One such usual and customary process is that meeting minutes be reviewed and approved by committee members before they become more broadly circulated. We also recommend the minutes include more detail including time, date, duration of meeting, who was in attendance, who was unable to attend, provide a record of what was said, what was agreed to, and list action items and their status.

Furthermore, in this case, it is particularly problematic because the minutes, in our view, and as confirmed by the observations we shared with you by email on August 9, 2018, do not accurately or completely reflect the discussions of the working group, which could mislead the reader regarding the degree of expert consensus on fundamental issues under consideration. This gap in the minutes limits the ability of external stakeholders to the TWG (i.e. PMPRB steering committee members) to understand the origin and rationale of the points of contention that the chair is required to record in the final report of the TWG (as per terms of reference).

As examples of the issues of concern to us, we would draw your attention to the following

passages:

- “Several members expressed the view that the opportunity cost of a drug may not be an appropriate tool for screening purposes. It was suggested further study may be needed to inform the discussion. Members generally agreed that application of supply-side cost effectiveness thresholds were an appropriate approach to consider opportunity cost when setting ceiling prices for Category 1 drugs”

    - In our view, there was no general agreement on cost effectiveness thresholds as an appropriate approach to consider opportunity cost and the TWG never resolved the issue of how such a threshold could be determined. There was in fact considerable debate and disagreement on this, leading to PMPRB Chair Mitch Levine to question potential alternatives to the use of pharmacoeconomics. This lack of consensus was evident from your proposal (and the PMPRB staff’s agreement) to schedule additional conference calls beyond what was planned in the terms of reference to allow for further discussion and to arrive at more aligned views.

- “Members discussed using the CADTH and/or INESSS reference case analysis to set a price ceiling, as well as potential approaches to take in situations where the existing reference case was not relevant.”

    - We would note that the meeting minutes should reflect that there was fairly widespread agreement that INESSS and CADTH assessments are NOT appropriate as reference cases, that the processes in place do not represent a peer-reviewed approach nor are they conducted from a perspective that is appropriate for price setting. Further, as representatives of our industry, we clearly communicated that the HTA cost-utility point estimates will never provide the level of certainty necessary and appropriate for the purposes of price setting within a quasi-judicial context.

We wanted to bring our concerns to your immediate attention and would welcome further discussion and validation of detailed meeting minutes with the working group. To ensure full transparency, we also want this email as well as our email of August 9 to be posted on the BrightShare site so that the Steering Committee members are able to appreciate our views.

We are happy to discuss either of these points if you have any questions, and looking forward to hearing from you to get your perspective on these issues. Thanks.

Geoff and Frederic

# Appendix 3.3: Email from Frédéric Lavoie and Geoff Sprang (3/4)

*Subject: Next steps for the PMPRB Technical Working Group*

*Date: 17 August 2018 at 11:17 MST*

*From: Frédéric Lavoie*
*To: Mike Paulden*
*Cc: Edward Burrows, Douglas Clark, Guillaume Couillard, Isabel Jaen Raasch, Matthew Kellison, Nelson Millar, Richard Lemay, Tanya Potashnik, Theresa Morrison, Geoff Sprang, Marie-Claude Aubin, Sylvie Bouchard, Chris Cameron, Christopher McCabe, Donald Husereau Doug Coyle, Karen Lee, Maureen Smith, Patrick Dufort, Peter Jamieson, Stuart Peacock, Tammy Clifford, Tania Stafinski*

Dear Mike,

Firstly, we would like to acknowledge and thank you Mike for the manner in which you have conducted and chaired this working group, maintaining a constructive and professional tone throughout the meetings and calls, despite the widely divergent views of the various group members.

As you and the other working group members know from our repeated reminders, the industry has a fundamental disagreement with the premise of using of the proposed economic factors to establish ceiling prices in the context of the PMPRB's mandate. Chief among those concerns are the difficulties of establishing the so-called "bright lines" which PMPRB itself has identified as an important element of the new regulatory framework, given the inherently subjective nature of point estimates, as well as the technical and operational challenges associated with implementation. These concerns make it very challenging for us to confine our commentary within the very narrow boundaries established by the terms of reference of the Working Group.

Although we have been repeatedly reminded by the PMPRB staff that the mandate of this WG is limited to finding solutions to implement the economic factors proposed in the draft regulations published through the Canada Gazette I process on the assumption that the final regulations published in the Canada Gazette II will be unchanged, we strongly believe it is our responsibility to call attention not only to the issues related to uncertainty and lack of clarity, but also to the significant and, in many cases, insurmountable technical and operational issues associated with the application of these economic factors. We appreciate that many of these issues have also been acknowledged in the perspectives and comments offered by other WG members.

Much if not all of the effort expended by the Working Group in arriving at recommendations will be of limited utility if technical or operational issues render them impossible or impractical to implement. For this reason, we feel strongly that to be informative, the group's recommendations need to be accompanied by comprehensive commentary on the known and potential technical and operational complexities of implementation.

In addition to participating in the initial Working Group meeting on July 26th, we have now attended all of the 8 hours of conference calls scheduled on August 22 and 24, 2018. It would have been helpful to hear from key stakeholders, such as CADTH staff, who were unfortunately not present during these calls. Through all of these discussions what is consistently apparent to us is that there is little if any consensus around the use of economic factors beyond using a set of international pricing reference tests in the regulatory ceiling price-setting exercise.

Despite the many hours of discussion, it appears that the application of the economic factors proposed by PMPRB to the working group remains associated with a lack of clarity. We have heard that this lack of clarity can be accommodated and may in fact provide a desired level of flexibility where economic factors are applied at the level of budget holders to guide decision making. However, in the context of their application in a prescriptive manner to establish an explicit ceiling price, given PMPRB's role as a price ceiling regulator, such a lack of clarity constitutes a critical limitation. Our working group discussions to date have only served to heighten our concerns that the uncertainty associated with their use and interpretation is significant and will not provide a bright line conducive to innovative companies understanding the implications of engaging within the Canadian market the significant resources required to commercialize innovations.

While we are cognizant of the limited terms of reference for this working group prescribed by the PMPRB, we feel it is our responsibility to reiterate to policy makers our strong recommendation that the working assumptions of the WG be revisited and that the Government of Canada urgently establish discussions with our industry to consider alternative regulatory approaches excluding the use of economic factors.

Below are our observations from the working group discussions about each of the six topics in scope that support the above industry perspective:

**DRUGS IN CATEGORY 1:**

- The industry is favourable to a risk-based approach to PMPRB's regulations;.one that is commensurate to the risk of abuse of a patentee's monopoly power. However, this risk categorization cannot be the gate towards the implementation of economic factor adjustments as currently intended in the current draft regulations (use of pharmacoeconomic price tests).

- The initial intent published by PMPRB that categorization of risks is framed on the basis of products having a cost-utility point estimate greater than $30,000/QALY (corresponds to a supply side estimate of UK willingness to pay threshold) would capture >90% of current patented medicines in Canada.

- The technical difficulty in establishing a cost-utility estimate for a newly launched medicine led the WG to discourage PMPRB for using this as a criterion to define risk.

- The WG thought that this exercise should exclusively include treatment cost per year, market size and degree of innovative value (breakthrough product).

- Preliminary data on risk-based categorization were only verbally shared with the WG by PMPRB staff. Further details and discussion is required before any conclusions could be made.

- The sensitivity of these criteria also needs to be evaluated post application of the first price test of international price referencing. This was not accounted for by PMPRB during its preliminary analyses.

**SUPPLY-SIDE THRESHOLD:**

- Industry representatives have repeatedly pointed out that the lack of precision (high levels of uncertainty) associated with cost-effectiveness estimates and thresholds of willingness to pay makes the use of these tools inappropriate for price ceiling determinations. This concern has been echoed by patient and HTA representatives. There does appear to be consensus that cost-effectiveness estimates and willingness to pay thresholds are (and should continue to be) used by payers to guide the allocation of limited resources within the preview of budget holders (public and private payers).

- The debates of the WG highlighted that there are various quantitative methods (supply-side and demand-side) that would yield differing estimates of willingness to pay of Canadians all susceptible to uncertainty and therefore open to be debated by stakeholders. Such a subjective estimate is not an appropriate tool to use in a quasi-judicial price ceiling setting exercise.

There was general agreement within the WG that PMPRB's initial position on UK supply-side estimate ($30,000/QALY) was not appropriate and some academic members of the WG suggested more Canadian specific research would need to be conducted before application in this setting and that status quo be observed until conclusion of Canadian research in this area (pause on the application of the economic factors).

- Another area of contention was raised in the WG deliberations as there is misalignment between the suggestions of PMPRB staff to use a supply side estimate of the Canadian willingness to pay threshold while the mandate of PMPRB is to protect the interests of Canadian consumers, aligning with a demand-side willingness to pay threshold quantitative method. Beside this unresolved issue, the use of demand-side thresholds could necessitate that the PMPRB run as many studies to establish thresholds as there are budget holders within the fragmented Canadian pharmaceutical system. Variability across multiple thresholds will also likely raise questions amongst patient stakeholders as to why certain areas and/or diseases are confronted to a lower threshold than other areas and/or diseases. There are many such ethical questions that have not been studied as part of Health Canada and the PMPRB's proposals.

- The uncertain nature of any cost-effectiveness threshold would represent an unrealistic reference for an innovative patented pharmaceutical tested against its equally uncertain cost-utility value.

**MARKET SIZE:**

- Mitigating the risk of budget impact is an objective of public and private payers in Canada. These stakeholders have effective tools to address the perceived risk pertaining to the anticipated market size a medicine would detain.

- It was acknowledged that use of a gross (or even net) sales number to make ceiling price adjustments ignores the actual budget impact which is more important to payers and which is also a more appropriate consideration in terms of rewarding innovation and influencing the allocation of resources. However, there is no practical or effective way to actually prospectively define this factor and any methodology used to forecast this factor would be accompanied by enormous uncertainty. It is also important to note that such factors are already routinely addressed at the level of budget holders through product listing agreements.

- Establishing a price ceiling threshold based on GDP factors is also problematic given economic variability and more importantly differences across jurisdictions and payer segments in definitions of affordability as well as local or regional healthcare priorities. Affordability and healthcare priorities are ultimately policy decisions best left with

individual jurisdictions. Such considerations are already addressed via existing government mechanisms (e.g. pCPA)

- Notwithstanding the industry opposing position, if pharmacoeconomic factors were implemented, why would patentees need to have their prices adjusted further for market size if they are delivering more value for money as use increases? Operationally, when does this adjustment happen?

**MULTIPLE INDICATIONS:**

- The uncertainty associated with potential in-market price adjustments resulting from the introduction of new indications or changes in the mix of business resulting from changes in medical practice or competitive dynamics would discourage manufacturers from launching new indications and make it more difficult to make launch decisions for Canada, thereby resulting in delays or potentially loss of access to innovative medicines.

- The practical limitations of tracking and reporting by indication make implementation effectively impossible in the context of the current Canadian prescription drug setting.

- Even in a hypothetical context when a subsequent indication of an already approved medicine would be associated with a higher cost-utility, there is no mechanism in place to implement differential pricing on a per indication basis. Furthermore, the behaviour of payers in reimbursement negotiation appears to follow a price-volume rationale over medicines' life cycle.

**PERSPECTIVE:**

- The societal perspective is the broadest perspective theoretically speaking but it is associated with important technical measurement hurdles. In a societal perspective, the evaluation of indirect costs has been the subject of important equity issues due to their discriminatory nature. The valuation of productivity through indirect costs often yields to the prioritization of treatments predominantly destined to working age Canadians at the expense of those targeting an older population more likely retired from the work force.

- Again, the expression of a bright line for price ceiling setting of pharmaceuticals would be blurred as a result of the lack of clear consensus in the academic community on which perspective is best, how to measure it adequately and how to shelter it against the accusation of it leading to discriminatory practices. These issues will make it difficult for the WG to come up with a meaningful recommendation.

**ACCOUNTING FOR UNCERTAINTY:**

- Regulating ceiling prices on the basis of factors that would be measured through payer processes not intended for price setting are a cause for concern. This was raised by the WG during the discussion on uncertainty.

- CADTH and/or INESSS that would produce cost-utility point estimates for medicines in Canada often exhibit differences in their estimates pertaining to heterogeneous assumptions and expert opinions. Their processes do not incorporate state of the art validation steps and levels of peer-reviews.

- The WG discussed the option of creating a new health economics committee to provide enhanced rigour in the evaluation. However, it was noted that the important shortage of trained health economist experts in Canada would make the composition of such group difficult and duplicative. This would also add another layer of complexity and delays on the already difficult Canadian journey of a pharmaceutical innovation.

The compounded uncertainty across multiple proposed economic factors is contrary to the PMPRB's stated objective of providing innovators with a bright line in forecasting ceiling prices of innovative entrants in the Canadian market.

As the working group moves to the next steps, it will be helpful to get clarity on the process for developing recommendations and the role of the PMPRB Steering Committee (SC) in this regard. We have been informed that the PMPRB staff clarified at the last SC meeting that the role of the SC is not to steer the work of the working group. This raises a serious governance and procedural question regarding the next steps in the process of development of any recommendations through the working group and the role of the SC in approving the recommendations.

Thanks in advance for the work you will do to fully integrate are above considerations into the WG's outputs.

Sincerely,

Frederic & Geoff

# Appendix 3.4: Email from Frédéric Lavoie and Geoff Sprang (4/4)

*Subject: Feedback related to September 25 meeting*

*Date: 3 October 2018 at 13:55 MST*

*From: Frédéric Lavoie*
*To: Mike Paulden*
*Cc: Geoff Sprang, Marie-Claude Aubin, Sylvie Bouchard, Christopher McCabe, Donald Husereau, Doug Coyle, Karen Lee, Maureen Smith, Patrick Dufort, Chris Cameron, Peter Jamieson, Stuart Peacock, Tammy Clifford, Tania Stafinski, Edward Burrows, Douglas Clark, Guillaume Couillard, Isabel Jaen Raasch, Matthew Kellison, Nelson Millar, Richard Lemay, Tanya Potashnik, Theresa Morrison*

Dear Mike,

In follow up to our Technical Working Group call on September 25th, and as the representatives of the industry subject to the PMPRB's guidelines, we wanted to capture and convey to you our key takeaways from the discussion as well as our understanding of next steps.

Once again, we want to commend you for your thoughtful and inclusive approach to a complex and challenging process given the limiting terms of reference set by PMPRB for the Working Group and diversity of views represented in the group. While we have provided some additional commentary specific to the six pre-specified areas below, it was apparent to us that we are still struggling to arrive at a consensus in any of these six areas and we appreciate your candor in acknowledging this at the close of the meeting. As we have stated repeatedly, the heterogeneity of opinions within the working group and the inability of the group to forge a consensus when it comes to the application of economic factors to price regulation is illustrative of the issues that form the basis of the regulated industry's concerns; specifically the degree of uncertainty, the lack of "bright lines" and the complexity of implementation which in our view represent critical limitations of the proposed regulatory framework.

We understand that the proposed next steps are the circulation of a draft report by October 5th for review by members prior to a final meeting of the Working Group on October 12th at which voting on the final recommendations will take place. Materials provided to you in advance of October 5th may be incorporated into the draft report. However, those provided after issuance of the draft report may still be considered at the October 12th meeting. The Final Recommendations of the Working Group will be issued at some point shortly thereafter to the Steering Committee for consideration in late October. However, the Steering Committee will not see any draft materials or commentary from the Working Group. Given the complexity of the

issues, we believe that the Working Group does not have sufficient time to complete its work in the timeframe defined by PMPRB.

Given that the Working Group's Terms of Reference state that recommendations will be determined by a simple majority vote, and in view of our comments above, we anticipate that arriving at a single set of coherent recommendations that "do justice" to the complexity of the issues will be extremely challenging and that what is ultimately presented to the Steering Committee may fail to reflect the underlying heterogeneity of opinion. Under these circumstances, we believe it is critical that the questions that will be subject to a vote, the process by which all of the results will be captured and reported, as well as the content and format of what will be shared with the Steering Committee and other relevant stakeholders be well defined in advance. We would therefore ask that these considerations be drafted and shared with the Working Group as soon as possible and before the voting process is launched. The Working Group members should be allowed to comment on the proposed process prior to undertaking any voting. We take comfort with your commitment of filing in the appendix of the final report the written comments of the Working Group members who wish them to be "on record". As such, please consider this email "on record".

In addition, and for reasons outlined previously, we believe that it will be important for stakeholders reviewing the output of the Working Group to be provided with information relating to the technical feasibility and other implementation issues and challenges associated with recommendations. It was our understanding from discussions at the September 12th meeting that PMPRB staff were to provide case studies to inform the Working Group's deliberations and we are disappointed that they have not done so to date. The suggestion from PMPRB staff that Working Group members with expertise and examples may bring these forward has come in the final weeks of the group's deliberations and provides an insufficient opportunity for their development and consideration. As industry representatives, and although we believe that it should be the responsibility of PMPRB staff as opposed to Working Group members to provide case studies, we will attempt to compile some case studies to share with the group in advance of our next meeting.

With respect to the six specific areas for consideration, as noted previously we do not support the inclusion of economic factors in a quasi-judicial price ceiling regulatory methodology given the uncertainty these would introduce, the practical challenges and complexity of implementation and the fact that the government's regulatory objectives can be achieved by much simpler, more transparent and predictable mechanisms. Our observations of the group's discussion are provided below.

1. Perspective – while some members expressed the view that a health system perspective would be preferable to a societal perspective in order to minimize discriminatory bias (e.g. productivity considerations), other members raised the concern that the health system perspective fails to account for the private for-profit

segment of the market. The concern that private payers are “profit-maximizers” and that potential price reductions may not be passed on to consumers has also been raised.

2. Threshold – there were differing points of view on whether the thresholds should be determined by supply side or demand side considerations. There was also a view that PMPRB cannot “enforce” or regulate efficiency and WTP varies, so it may be better to set an upper limit on all but let payers negotiate. There was some support for additional empirical work as general agreement that thresholds used in existing HTA assessments would not appropriately reflect collective WTP. The need for further research in this area in which current empirical work is insufficiently mature and not Canada specific has also been raised.

3. Uncertainty – Uncertainty is reflected in HTAs and resulting decision making by considering the range of possible ICERs rather than a point estimate. HTAs are not performed with the objective of determining a point estimate for price setting. New drugs are introduced and priced at the point of maximum uncertainty which typically declines over time.

4. Market Size – recognition of the fact that net budget impact is more important than gross sales; challenges in defining this ex ante given uncertainty in forecasting.

5. Multiple Indications – general agreement that pricing by indication is theoretically appealing, it is not possible given current limitations in data capture and reporting. Practically it seems necessary to regulate one price across indications, however there was no agreement on how a single price across indications would be established.

6. Category 1 Criteria – general agreement that CE would not be appropriate screening criteria, support for risk based approach, some support for use of level of therapeutic improvement and new MOA as a consideration, concerns expressed about market size vs net budget impact as this could distort screening, also concerns expressed about impact of a specific threshold on orphan drugs.

We look forward to your response. If you have any questions, please do not hesitate to contact us.

Regards,

Geoff and Frederic

# Appendix 3.5: Summary comments from Frédéric Lavoie and Geoff Sprang

*Date: 1 March 2019 at 15:00 MST*

As members of the Technical Working Group (TWG) representing BIOTECanada and Innovative Medicines Canada, we wish to enter the following summary of observations and issues into the record on behalf of our respective memberships, who represent most of the patentees subject to the PMPRB's jurisdiction.

As both organizations have previously communicated, we believe the use of the proposed economic factors in the context of quasi judicial price regulation is inappropriate. Our concerns in this regard and the underlying rationale have been captured elsewhere and for that reason are not restated here but can be reviewed under on the record comments in the appendix of the TWG report. However, our participation in the TWG and the opportunity to further explore the complex issues associated with the use of economic factors in this way has only served to reinforce our concerns that these reforms will, at best, delay access to new therapeutic options for Canadian patients, and potentially impede access altogether to the extent that manufacturers elect not to launch new therapeutic products in Canada.

Overall, a key concern was lack of clarity around the overarching policy objectives. In a number of cases the TWG was unable to arrive at clear recommendations and ultimately determined that the questions posed could only be answered with further clarification of PMPRB's policy objectives. The fact that such objectives were not sufficiently clear to the TWG is in and of itself problematic and limited the value of the TWG. We also note that the deferral within the proposed recommendations to "policy intent" should not be construed as support for the proposed new economic factors.

Another important and challenging topic for TWG consideration was Topic 5 – Perspective which, under the Terms of Reference, required the TWG to discuss options to account for the consideration of a public health care system versus a societal perspective. Given the heterogeneous nature of the Canadian payor landscape, which includes public payors, employer-sponsored privately funded plans as well as cash paying customers, discussions of this topic reflected very divergent views. It is disappointing and, in our view, inappropriate that, having asked the TWG to provide advice, the PMPRB intervened and imposed the decision to adopt a public health care system perspective without regard to the diverse views of the expert members of the TWG.

In addition, we believe that the Terms of Reference for the TWG greatly limited the value of the exercise in leveraging both the practical and academic expertise of the members. For example,

we feel it is important to register our concern and disappointment that important feasibility issues related to implementation were considered out of scope; particularly as the TWG is the only forum specifically charged with consideration of technical questions related to implementation. We find it inconceivable that the proposed regulatory reform process has reached this stage without having given due consideration to technical feasibility.

Our efforts to call out significant feasibility challenges were essentially dismissed by PMPRB staff. In some cases the feasibility issues that we attempted to raise are substantive enough that patentees subject to the proposed regulation changes do not currently have the ability to comply with the new reporting requirements. In other cases, our compliance with the proposed reforms would have major implications for resourcing and enterprise system reconfiguration adding enormously to the existing cost and regulatory burden of reporting by patentees. Significantly adding to the regulatory burden without due consideration to alternative regulatory options makes no sense and runs counter to the federal government's efforts to reduce so-called "red-tape".

We also want to register our concern that despite numerous requests and emphasis on the need for case studies to be developed to explore how the proposed reforms would be applied, case studies were only made available in the final stage of the TWG deliberations and a review and discussion of all 6 individual case studies was allocated only 35 minutes on the agenda of the one meeting where they were discussed. A robust discussion of these case studies would have added greatly to the TWG's deliberations. The case studies themselves, which were developed by the PMPRB, raise numerous issues that are illustrative of the kinds of challenges that will arise if the current regulatory revisions are implemented as proposed. It is noteworthy that despite significant efforts within our respective trade associations as well as the use of external pricing and analytical expertise, we were unable to reverse engineer or replicate the PMPRB's results. This is concerning in and of itself and underscores the need for additional consultation. The magnitude of price reductions illustrated by the case studies also raises concerns since it is clearly not aligned with the Regulatory Impact Analysis Statement and Cost-Benefit Analysis released by Health Canada with the draft regulatory amendments or with the objective of aligning Canadian prescription drug prices with those of a broader subset of reference markets. When these issues were raised at the TWG they were not adequately addressed by PMPRB staff.

Overall, while we appreciate the efforts of the Chair (Mike Paulden) to execute the mandate he was given as impartially as possible, the mandate itself (Terms of Reference), the limitations placed on the scope of the TWG's considerations (notably the exclusion of considerations of technical feasibility), the lack of clarity early in the process surrounding the PMPRB's policy intent that limited the TWG's ability to provide meaningful recommendations in many areas, the late availability and insufficient time allocated to the consideration of case studies and the decision of the PMPRB to disregard the TWG's deliberations of Topic 5 (Perspective), combined to render the TWG exercise inadequate as a consultation process.

As representatives of the innovative industry, we have clearly acknowledged the challenges facing governments in meeting the expanding healthcare demands and we reiterate our willingness to work with governments and other stakeholders to find appropriate solutions. These solutions must reflect a comprehensive and balanced policy framework that extends beyond pharmaceutical price ceiling controls to include the objective of ensuring Canadians have timely access to the best treatment options and to preserving Canada's attractiveness as a destination for life sciences research and investment. Therefore, as it relates to price ceiling regulatory reforms, we continue to advocate for more robust consultations with representatives of industry, patient associations, other federal government ministries as well as provincial governments, all of whom share the objective of improving the health and well-being of Canadians.

# Appendix 3.6: Summary comments from Maureen Smith

*Date: 1 March 2019 at 15:59 MST*

As a member of the Technical Working Group, I would like the following comments to be included in the appendices of the Technical Working Group (WG) Final Report. When I accepted the invitation to join the PMPRB's Technical Working Group in July 2018, I knew that it would be challenging to provide my own patient perspective in a Working Group whose purpose was to inform the PMPRB Steering Committee on the modernization of price review process guidelines. After all, not many patients know about this quasi-judicial body that sets price ceilings for patented drugs in Canada, yet these ceiling prices are important to patients as they can have consequences on the sustainability of our health care system and access to medications. I have spent the past five years as a patient member of a provincial health technology assessment body, therefore, I felt that I had enough understanding of health economics to participate in the discussions and hopefully bring my lived experience as a Canadian with a rare disease who relies on drugs and has dealt with access issues.

Unfortunately, I believe that the WG was not able to engage in a discussion that would have allowed us to deliver on our terms of reference. Simply put, the terms of reference were not reflective of the scope of the Technical WG. Much of what we were tasked to discuss in the six areas of focus was pre-determined by the Regulatory Impact Analysis Statement (RIAS) that were published in the Canada Gazette, Part 1. For example, after two months of discussion on the options to account for the consideration of a public health care system versus societal perspective, the WG was informed by the PMPRB that, as stated in the RIAS, they were adopting a public health care system perspective. Why then was the WG ever asked to discuss perspective? Given that we do not have a national pharmacare program in Canada and that Canadian consumers use public plans, private insurance, or pay out of pocket for their drugs, it was disappointing that the perspective had already been determined.

The WG was told that other topics were out of scope as well, despite a terms of reference that suggested otherwise. While I appreciate that we were not there to debate the RIAS, the terms of reference should have been more aligned with the RIAS and its constraints. Another barrier to fulfilling our mandate was the lack of a proper review of empirical evidence on each topic. This should have been undertaken, rather than relying on WG members' own knowledge of what was available and personal biases. Finally, as early as the first meeting and then repeatedly several WG members requested that the PMPRB develop case studies that would allow us to work through the technical details and have a better understanding of the impact. Case studies that were developed for the Steering Committee were finally made available to us and we were granted 30 minutes to discuss this during our final meeting.

The recommendations you see will most likely have a high degree of agreement because, except for a few, they cannot truly be considered recommendations if one looks at the specific questions in our six areas of focus. They are a record of whether the members of the WG agree on our conclusions. There really isn't much to disagree on, since no resources were invested in synthesizing the existing empirical evidence, resulting in little space for a thoughtful technical discussion. As I see it, the WG's recommendations fall into five categories: (1) advising the PMPRB to adopt measures that will be consistent with their policy intent; (2) recommendations that simply state that this is the only option because of the policy intent; (3) those that deal with the enormous challenges of applying health technology assessment to a country with 17 jurisdictions who each have their own drug budgets and priorities; (4) recommendations that state the WG's conclusions such as 2.3 "The WG regards the direction and magnitude of any bias in the $30,000 per QALY estimate by Ochalek et al. (2018) to be unknown"; and (5) recommendations that call on further empirical research. For me, this is the result of 31 hours of discussion and, unfortunately, the impact is minimal due to the failure in the process.

As a patient, my goal was to contribute to the discussion of achieving the fine balance that doesn't discourage market access while charging prices that payers feel will protect the public health system. Patients are concerned about the prices of drugs but they are also concerned about having access to innovative therapies in Canada. There is some evidence that countries such as Australia and New Zealand who have some of the toughest drug prices have less access. Another concern is whether the application of health technology assessment tools by the PMPRB will result in further inequity in access to drugs for Canadians, especially for those relying on drugs for rare diseases whose coverage is often determined by their postal code. Will they acknowledge the challenges of HTA for rare disease drugs, especially the inappropriateness of thresholds? Finally, if the PMPRB expands its mandate to integrate HTA into setting ceiling prices, they should have a process for patient input into their work similar to the patient submission processes that our Canadian HTA agencies have adopted.

In conclusion, it is my opinion that the PMPRB missed an opportunity to truly consult the WG members as much of the outcome was pre-determined by the key guideline document (the RIAS) and there was a lack of clarity on the policy intent from the outset. It is worrisome that the Technical WG was not able to debate the important considerations and reduce some of the uncertainty in what the consequences will be for Canadian patients by making recommendations that would have reflected our best thinking.

# Appendix 4: Terms of Reference

# Terms of Reference for Working Group to Inform the Patented Medicine Prices Review Board (PMPRB) Steering Committee on Modernization of Price Review Process Guidelines

## Background

The Patented Medicine Prices Review Board (PMPRB) recently established a 'Steering Committee on Modernization of Price Review Process Guidelines'. The mandate of this **Steering Committee** is to assist the PMPRB in synthesizing stakeholder views on key technical and operational modalities of the PMPRB's new draft Guidelines.

The Steering Committee's work will be based in part on the analysis and recommendations of a technical **Working Group**, which will examine certain issues that the Steering Committee believes would benefit from the review of experts in health technology assessment and other economic and scientific matters.

The Working Group will comprise leading experts in pharmacoeconomics and the clinical evaluation of pharmaceuticals. The Working Group will meet twice in-person and multiple times via tele-conference between July and October 2018. A report of the Working Group's deliberations and recommendations will be produced by the chair and submitted to the Steering Committee for consideration in October 2018.

## Membership

The chair of the Working Group will be Dr Mike Paulden (University of Alberta).

Thirteen individuals will sit as members of the Working Group (listed alphabetically):

1. Sylvie Bouchard (Patrick Dufort as alternate if needed) (INESSS);
2. Dr Chris Cameron (Dalhousie University and Cornerstone Research Group);
3. Dr Tammy Clifford (University of Ottawa and CADTH);
4. Dr Doug Coyle (University of Ottawa);
5. Don Husereau (University of Ottawa);
6. Dr Peter Jamieson (University of Calgary);
7. Dr Frédérick Lavoie (Pfizer Canada);
8. Dr Karen Lee (University of Ottawa and CADTH);
9. Dr Christopher McCabe (University of Alberta and Institute of Health Economics);
10. Dr Stuart Peacock (Simon Fraser University and BC Cancer Agency);
11. Maureen Smith (Patient);
12. Geoff Sprang (Agmen);
13. Dr Tania Stafinski (University of Alberta).

Two individuals will sit as observers of the Working Group:

1. Edward Burrows (Innovation, Science and Economic Development);
2. Nelson Millar (Health Canada).

One individual will act as an external reviewer of the Working Group's draft report:

1. Dr Mark Sculpher (University of York).

Recommendations of the Working Group will be determined by a vote of the members. In the event of a tie, the chair will have the casting vote.

# Areas of focus

The Working Group will examine and make recommendations with respect to the following considerations and questions:

**1. Options for determining what medicines fall into 'Category 1'**

- A Category 1 medicine is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing.

- The following criteria have been identified as supporting a Category 1 classification:

    a) The medicine is 'first in class' or a 'substantial' improvement over existing options
    b) The medicine's opportunity cost exceeds its expected health gain
    c) The medicine is expected to have a high market impact
    d) The medicine has a high average annual treatment cost

- Should other criteria be considered? What are the relevant metrics for selecting medicines that meet the identified criteria and what options exist for using these metrics?

**2. Application of supply-side cost effectiveness thresholds in setting ceiling prices for Category 1 medicines**

- Potential approaches for implementing a price ceiling based on a medicine's opportunity cost.

- Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc)

**3. Medicines with multiple indications**

- Options for addressing medicines with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).

**4. Accounting for uncertainty**

- Options for using the CADTH and/or INESS reference case analyses to set a ceiling price.

- Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.

**5. Perspectives**

- Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a 'significant' difference between price ceilings under each perspective.

- How to define a 'significant' difference in price ceilings between each perspective.

**6. Application of the market size factor in setting ceiling prices**

- Approaches to derive an appropriate affordability adjustment to a medicine's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' approach).

Additional areas of focus may be identified by the Steering Committee prior to the first meeting of the Working Group in July 2018.

It is anticipated that the approaches or methods recommended by the Working Group may not be identical to approaches or methods currently employed by CADTH or INESSS. Where such departures present potential hurdles for operationalization of its recommendations, the Working Group will identify potential technical or other solutions to these hurdles.

## Confidentiality

Working Group members may consult with non-members on an ongoing basis but are expected to maintain the confidentiality of any materials provided to them during the course of their work.

The names of the members of the Working Group will be published on the PMPRB's website, along with a report of its deliberations, analysis and recommendations.

## Governance and procedure

It is recognized that members of the Working Group may hold opposing points of view on the above issues and/or disagree with the policy rationale underlying the changes to the PMPRB's Guidelines. Members are nonetheless encouraged to work together constructively to assist the Working Group in carrying out its function.

The chair is expected to foster consensus among members, but in order to ensure that Working Group deliberations are as focused and productive as possible, the chair shall have final say on all matters of governance and procedure. Members who disagree with a decision of the chair in this regard can request that their objection be noted on the record. The chair shall make every

effort to ensure that the Working Group's final report accurately reflects any important points of convergence or contention between members.

## Schedule

The Working Group will meet for the first time in-person in Ottawa in July, followed by numerous tele-conferences in August and September. Following submission of a draft report, a second in-person meeting will be held in October.

All dates are subject to the availability of the chair and members of the Working Group.

| **Date** | **Event** | **Purpose** |
|---|---|---|
| 26 July 2018 | Full day in-person meeting in Ottawa | Overview of Working Group objectives. Summary of specific areas of focus under consideration. Allocation of tasks among Working Group members. |
| 22-24 August 2018 | One-hour teleconference on each area of focus | Opportunity for input from Working Group members. |
| 24 August 2018 | Two-hour tele-conference | Update on Working Group status. Opportunity for input from Working Group members. |
| Week of 10 September or 24 September 2018 (TBC) | Two-hour tele-conference | Update on Working Group status. Opportunity for input from Working Group members. |
| 5 October 2018 | Draft report circulated among PMPRB staff and Working Group members | Opportunity for input from PMPRB and Working Group members. |
| 12 October 2018 | Full day in-person meeting in Ottawa | Present draft report. Report draft recommendations. Final opportunity for input from PMPRB and Working Group members. |
| 26 October 2018 | Final report delivered to PMPRB | Final deliverable to PMPRB. |

## Deliverables

A draft report will be circulated among PMPRB staff and Working Group members on 5 October 2018, prior to the final in-person meeting in Ottawa. A final report will be submitted to the PMPRB on 26 October 2018 and circulated among Working Group and Steering Committee members.

Following delivery of the final report, the chair will be willing to present the recommendations of the Working Group to stakeholders and other interested parties, subject to availability.

## Budget

The PMPRB may cover reasonable travel and accommodation costs of members where such funding is requested and approved in advance. Where possible, the chair of the Working Group will arrange meetings to attempt to minimize expenditures for participants.

# Appendix 5: Policy Intent

# Appendix 5.1: Regulations Amending the Patented Medicines Regulations

Vol. 151, No. 48 — December 2, 2017

# Regulations Amending the Patented Medicines Regulations

**Statutory authority**

*Patent Act*

**Sponsoring department**

Department of Health

## REGULATORY IMPACT ANALYSIS STATEMENT

(*This statement is not part of the Regulations.*)

### Executive summary

**Issues:** The Patented Medicine Prices Review Board (“PMPRB” or “the Board”) uses a regulatory framework that currently falls short of its mandate to protect Canadian consumers from excessive prices for patented medicines. Canada’s patented medicine prices are among the highest in the world, and despite significant changes in the medicine market, the *Patented Medicines Regulations* have not been substantively changed in over two decades. The Regulations need to be modernized to provide the PMPRB with more relevant and effective regulatory tools in order to better protect Canadians from excessive prices for patented medicines.

**Description:** This proposal would amend the *Patented Medicines Regulations* (“Regulations”) so that the PMPRB’s regulatory framework includes new price regulatory factors and patentee price information reporting requirements that will help the PMPRB to protect Canadian consumers from excessive prices. There are five elements.

*New price regulatory factors and updating the schedule of comparator countries*

(1) Providing the PMPRB with three new price regulatory factors to enable it to consider the price of a patented medicine in relation to its value to patients and impact on the health care system.

(2) Updating the schedule to the Regulations that sets out the countries (now the PMPRB7) on which patentees report pricing information to include countries with similar consumer protection priorities, economic wealth, and marketed medicines as Canada. This would provide the PMPRB with the information needed to regulate prices based on comparisons that are more closely aligned with the PMPRB's mandate and Canada's domestic policy priorities.

*New reporting requirements*

(3) Reducing reporting obligations for patented veterinary, over-the-counter and "generic" medicines (i.e. those authorized for sale by the Minister of Health through an Abbreviated New Drug Submission [ANDS]). As these products pose a lower risk of asserting market power and charging excessive prices, this reduction would enable the PMPRB to focus on medicines at higher risk of excessive pricing.

(4) Amending patentee price information reporting requirements to include reporting in relation to the new factors.

(5) Requiring patentees to report price and revenue information net of all price adjustments such as direct or indirect third party discounts or rebates. This would ensure that the PMPRB is fully informed of the actual prices for patented medicines in Canada and enhance the relevance and impact of domestic price comparisons.

**Cost-benefit statement:** The proposed amendments would produce an estimated net benefit to Canadians of $12.6 billion net present value (NPV) over 10 years due to reduced prices for patented medicines. Lower prices would alleviate financial pressures on public and private insurers and improve affordable access for Canadians paying out-of-pocket. Lost revenues to industry are estimated to be $8.6 billion present value over 10 years. Costs to industry are estimated to be $9K/year in total, including administrative and compliance costs. Government costs of approximately $8.8M/year (PV) would include increasing the PMPRB's staff and resources for an anticipated increase in compliance and enforcement activities.

It is not anticipated that these amendments would generate adverse impacts on industry employment or investment in the Canadian economy. Although when the current regulatory framework was first conceived 30 years ago, policy makers believed that patent protection and price were key drivers of medicine research and development (R&D) investment, there is no evidence of this link. The level of industry R&D investment relative to sales by medicine patentees in Canada has been falling since the late 1990s and is now at a historic low despite Canada having among the highest patented medicine prices in the world. These amendments would aim to align Canadian prices with those in countries that, despite having lower prices, receive higher medicine industry investment.

**"One-for-One" Rule and small business lens:** The "One-for-One" Rule applies and the anticipated administrative burden is estimated to be $3,062 (2012 dollars) annually. The small business lens does not apply.

**Domestic and international coordination and cooperation:** Price regulations on medicines are a common international practice, although there is a significant variation in approach. These differences often arise from a need to tailor policy instruments to work within each

country's health care system. While countries monitor foreign models, it is to keep abreast of international best practices, rather than to harmonize. Regulating the prices for patented medicines to be non-excessive is not subject to trade provisions.

## Background

*Patented medicines are an important part of Canada's health care system*

Patented medicines help prevent and cure disease as well as save lives. But Canadians are not getting the value for money on prescription medicine spending or the outcomes they deserve. Medicine spending in Canada has increased from less than 10% of total health expenditure, when Medicare was first established 49 years ago, to about 16% today. Medicines are now the second-largest category of spending in health care, ahead of physician services and behind total hospital spending (which includes medicines used in hospital). Canadians are spending more per capita on medicines than any other country in the world, with the exception of the United States. Greater medicine expenditures can limit access to innovative medicines by straining the budget envelope for medicines of public and private insurers, place a financial burden on patients who pay out of pocket for their medicines, and mean fewer resources for other critical areas of the health care system.

In January 2016, federal, provincial and territorial ministers agreed to work together to improve the accessibility, affordability, and appropriate use of medicines to better meet health care system needs. The Government of Canada is committed to this work and is taking action to lower the cost of medicines, provide faster access to new medicines that are safe and effective, and support the development of tools for more appropriate prescribing. To support these actions, Budget 2017 outlined an investment of $140.3 million over five years, starting in 2017–2018, and $18.2 million, for ongoing years. The proposed regulatory amendments contribute to this initiative with respect to the price of patented medicines.

*The Patented Medicine Prices Review Board ("PMPRB" or "the Board")*

The PMPRB was created in 1987 as the consumer protection "pillar" of a major set of reforms to the *Patent Act* ("Act"), which were designed to encourage greater investment in medicine R&D in Canada through stronger patent protection. The Act sets out the period of time that patentees of a medicine are provided the exclusive rights granted by a patent. It also establishes the PMPRB as a quasi-judicial body with a price regulatory mandate to ensure that patentees do not abuse their patent rights by charging consumers excessive prices during this statutory monopoly period.

The Act and the *Patented Medicines Regulations* ("Regulations") together form the patented medicines price regulatory framework of the PMPRB. Regulations with respect to patented medicine prices and information are made pursuant to the Minister's recommendation; however, the PMPRB carries out its regulatory mandate at arm's length from the Minister.

## *The* Patent Act *and* Patented Medicines Regulations

Although no definition of "excessive" is included in the regulatory framework, it does specify the factors and information that the Board must consider in determining whether a price is excessive. The current price regulatory factors as set out in section 85 of the Act are the following:

- The prices at which the same medicine has been sold in the relevant market;

- The prices at which other medicines in the same therapeutic class have been sold in the relevant market;
- The prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada; and
- Changes in the Consumer Price Index.

The Regulations specify the price information that patentees must report to the PMPRB to allow it to regulate prices and report on trends. They include requirements to report the identity and price information for patented medicines sold in Canada and their prices in seven foreign countries where they are also sold. Currently the seven countries set out in the schedule to the Regulations (the PMPRB7) are the United States, the United Kingdom, France, Germany, Switzerland, Italy and Sweden. Although section 85 of the Act allows for further price regulatory factors to be prescribed in the Regulations, none have been proposed for consideration until now.

## *The PMPRB's* Compendium of Policies, Guidelines and Procedures

Many of the core regulatory concepts in the Act and the Regulations have been further developed in, and are operationalized through, guidelines. The PMPRB is authorized to make non-binding guidelines under section 96 of the Act, subject to consultation with relevant stakeholders. The purpose of the guidelines is to establish, and ensure that patentees are generally aware of, the policies and procedures undertaken by the Board staff to identify the medicines that might be priced excessively.

#### *How the current regulatory framework works*

Under the PMPRB's current regulatory framework, as operationalized through the guidelines, new patented medicines are assessed for the degree of therapeutic benefit they provide relative to existing medicines on the market. Depending on the outcome of that process, the PMPRB determines a price ceiling for new patented medicines that is based either on the median price of that same medicine in the PMPRB7 countries, the highest-priced medicine in Canada in the same therapeutic class, or some combination of the two. Once a patentee sets a medicine's introductory price in relation to that ceiling and it enters the market, the PMPRB allows annual price increases in keeping with the Consumer Price Index (CPI), provided these increases do not make the Canadian price greater than the highest price of the same medicine among the PMPRB7 countries.

The PMPRB's current regulatory framework is operationalized by Board staff who investigate medicines that appear to be priced excessively. Board staff apply the tests and thresholds specified in the guidelines to each patented medicine sold in Canada, notify the patentee that they are under investigation if the prices fail those tests and thresholds, and try to negotiate a voluntary compliance undertaking (VCU) by the patentee based on the compliant price level as set out in the guidelines. A VCU is a written commitment by a patentee to comply with the PMPRB's guidelines, including adjusting the price of the patented medicine in question to a level that complies with the guidelines and offsetting any potential excess revenues that may have been received as the result of having sold the patented medicine at a non-guideline compliant price in Canada.

If an acceptable VCU is not concluded, the case proceeds to a public adversarial hearing in front of a panel composed of members of the Board. During a hearing, the Board panel acts as a neutral arbiter between the parties (Board staff and the patentee). The Board panel must consider every factor under subsection 85(1) in determining whether the price of a medicine sold in Canada is excessive. The Board panel is not

bound by the guidelines during a hearing, although the Board staff, when presenting evidence in front of the Board, often relies on tests and methods that appear in the guidelines as part of its case that the medicine has been sold at an excessive price. If the Board panel determines that the medicine was sold at an excessive price, it may issue an order to enforce a non-excessive price and order the patentee to repay any excess revenue that resulted from selling the drug at an excessive price. An order of the Board can be enforced in the same manner as an order of the Federal Court.

*Canada's changing market and rising medicine costs*

Since the establishment of the PMPRB three decades ago, the medicine market has changed significantly. Medicine development is increasingly focussed on higher-cost medicines, such as biologics, genetic therapies targeted to smaller patient populations and medicines for rare diseases. The risk of asserting market power through excessive pricing is often greater for these products since there are few, if any, substitutes, and the patentee is not subject to competition. This is especially true for medicines that are first of their kind, or for which alternatives are less effective or have less tolerable side effects.

The current market dynamic has contributed to a significant increase in the cost of medicine in Canada which, if left unaddressed, is expected to continue. Between 2005 and 2016, the number of medicines in Canada with annual per-patient treatment costs of at least $10,000 increased from 20 to 135. This represents between 30% and 40% of new patented medicines coming under the PMPRB's jurisdiction each year and is a dramatic increase in these types of medicines over a brief timeframe. In 2015, 20 medicines had annual per-patient treatment costs over $50,000. High-cost specialty medicines now account for nearly one quarter of public and private insurer costs, but less than 1% of their beneficiaries.

Canadian patented medicine prices are among the highest in the world. Of all 35 Organisation for Economic Co-operation and Development (OECD) member countries, only the United States and Mexico have higher patented medicine prices than Canada. In 2015, median OECD prices for patented medicines were on average 22% below those in Canada.

*Confidential price adjustments*

Medicine manufacturers increasingly negotiate price adjustments with insurers in exchange for having their products reimbursed through insurance plans. These price adjustments are typically negotiated in confidence, with the agreement that they not be disclosed publicly. This means that there is a growing discrepancy between public list prices and lower actual prices paid in the market due to the increased use of confidential price adjustments.

*Limitations of current price regulation*

For the past 20 years, many countries that set price limits on medicines have relied on international price comparison between countries. With the emergence of higher-cost medicines, coupled with confidential price adjustments, countries have had to modernize with new methods that, for those medicines, are more reliant on assessing the economic value of a new medicine to their respective health systems and less on comparing prices internationally. Between 2010 and 2012, 23 European countries began planning or executed significant reforms to their regulatory frameworks for patented medicine prices. While international price comparison is still widely used in international price regulation, it is increasingly used as an adjunct to other pricing factors.

*Price regulatory factors*

Section 85 of the Act sets out the price regulatory factors that the Board must consider in determining whether a medicine is being or has been sold at an excessive price in Canada. The current price regulatory factors direct the Board to consider the prices at which a medicine or other medicines in the same therapeutic class have been sold in other countries. The PMPRB relies upon public prices when making price comparisons internationally; however, these public prices do not reflect the confidential price adjustments negotiated with some insurers that have become systemic in Canada and around the world. In an era marked by high-cost specialty medicines, the level of confidential price adjustments negotiated can be substantial. This means that there is a growing discrepancy between public list prices and lower actual prices paid in the market and leaves the PMPRB to regulate on the basis of public prices that bear less and less resemblance to what insurers are actually paying in the market. The PMPRB needs other factors that it can use to assess whether a price is excessive.

*The schedule of comparator countries*

The schedule to the Regulations sets out the seven countries for which patentees are to submit price information. The PMPRB uses the prices of the same patented medicines in these countries, where available, to set price limits on medicine prices in Canada at introduction and in subsequent years. The schedule of countries to the Regulations has not been updated since the Regulations were first conceived 30 years ago. At that time, policy makers believed that patent protection and price were key drivers of medicine R&D investment. The choice was made to offer a comparable level of patent protection and pricing for medicines as existed in countries with a strong medicine industry presence, on the assumption that Canada would come to enjoy comparable levels of R&D. However, the percentage of R&D-to-sales by patentees in Canada has been falling since the late 1990s and is currently less than Canada obtained at the time of the 1987 *Patent Act* reforms. By comparison, and despite Canada having among the highest patented medicine prices, industry R&D investment relative to sales in the PMPRB7 countries is on average 22.8% versus 4.4% in Canada. As a result, there is no evidence of a determinant link between domestic prices and the location of industry R&D investment. Other factors, such as head office location, clinical trials infrastructure and scientific clusters, appear to be much more influential determinants of where medicine investment takes place in a global economy.

The policy intent of the original schedule selection has not materialized and is no longer considered to be the most appropriate basis for the composition of the countries listed in the schedule. The regulatory requirements for patentees to report on prices in the PMPRB7 keep Canadian prices for patented medicines among the highest in the world.

## Issues

The Board determines whether a price is excessive based on the price regulatory factors in the Act, and the patentee price information reporting requirements specified in the Regulations. The evolution in the global and Canadian medicine environment has made apparent two important limitations to the Board’s current regulatory framework: (1) the ineffectiveness of the current price regulatory factors to adequately inform the PMPRB’s assessment of excessiveness; and (2) the insufficiency of the patentee price information reporting requirements.

Under the current regulatory framework, excessiveness is assessed almost entirely on the basis of domestic and international public list prices. This is problematic with an influx in high-cost specialty medicines and list prices not reflective of what public and private insurers are actually paying. The main limitations of the current framework are that

- It does not provide additional price regulatory factors, beyond price comparisons and CPI, for the PMPRB to assess whether a price is excessive. It does not consider whether the price of a medicine reflects
- **The value of a medicine to a patient:** medicines that offer substantial clinical benefits to patients or are alone in their therapeutic class will be in greater demand than medicines that are only marginally better than the standard of care or are one among many in their class;
- **The number of patients that can benefit from a medicine:** the size of the market for a medicine can have an impact on its expected price and the ability to pay for the medicine in a given country; and
- **The wealth of a country:** countries with greater economic resources can afford more or higher-cost medicines than countries with fewer resources.
- The list of countries used for price comparisons (PMPRB7) is out of date. Canadian prices for new medicines are compared to those of countries with high medicine prices, rather than to those of countries with similar medicine markets, consumer protection and wealth. The selection of countries can have a significant impact on the price maximums for patented medicines in Canada. As the PMPRB relies on international price comparisons, the PMPRB7 set of comparator countries has the effect of allowing higher prices in Canada than would otherwise be the case if comparator countries were more reflective of the Canadian medicine market.

### Objectives

The proposed amendments to the *Patented Medicines Regulations* would ensure that the PMPRB is equipped with the price regulatory factors and patentee price information reporting requirements necessary to fulfill its mandate to protect Canadian consumers from excessive prices for patented medicines. It is anticipated that the implementation of these amendments by the PMPRB would lead to lower prices for patented medicines in Canada that are more closely aligned with their value to patients and the health care system, and Canadians' willingness and ability to pay.

### Description

There are five elements included in the proposed amendments.

## Price regulatory factors and updating the schedule of comparator countries

1. Introduce new, economics-based price regulatory factors that would enable the PMPRB to ensure non-excessive prices that reflect value and Canada's willingness and ability to pay for patented medicines.

2. Update the schedule of countries used by the PMPRB for international price comparisons to be better aligned with the consumer protection mandate of the PMPRB and median OECD prices.

## Reporting requirements

3. Reduce reporting obligations for patented veterinary, over-the-counter and "generic" medicines.

4. Set out the information reporting requirements to enable the PMPRB to operationalize the new price regulatory factors.

5. Require patentees to report price and revenue information that is net of all domestic price adjustments such as direct or indirect third party discounts or rebates and any free goods or services.

A more detailed description of each of the proposed amendments follows.

## 1. Introduce new, economics-based price regulatory factors that would ensure prices reflect value and Canada's willingness and ability to pay for patented medicines

This proposed amendment would introduce three additional price regulatory factors of pharmacoeconomic value, market size, and gross domestic product (GDP) and GDP per capita in Canada. These new price regulatory factors would enable the PMPRB to consider complementary and highly relevant aspects of price excessiveness related to the value of the health benefit produced by the medicine, and the willingness and ability of Canadian consumers to pay for it. These new factors will only apply to sales of patented medicines that occur after the coming into force of the proposed amendments.

*Pharmacoeconomic value of the medicine in Canada*

The price paid for a medicine should take into consideration the value it produces. At the same time, it must recognize the cost to supply the medicine if manufacturers of medicines are to continue to invest in the production of new medicines. A pharmacoeconomic evaluation identifies, measures, and compares the costs and benefits of a given medicine to patients and the health care system. The inclusion of this factor would require the Board to consider whether a medicine's price is commensurate with the benefits it provides to patients within the context of the Canadian health care system.

*Size of the market for the sale of the medicine in Canada and in countries other than Canada*

The addition of this factor in the Regulations could enable the PMPRB to develop market impact tests for medicines that are likely to pose affordability challenges for insurers due to the market size for the medicine. The impact of an excessive price is a function of both price and volume; the larger the size of the market for the medicine in Canada, the greater the impact of its price. Where public and private insurers are called on to cover the cost of a medicine for a significant number of patients, the high cost of a medicine could render the medicine unaffordable for all who need it. The Canadian price could be assessed against international prices and prevalence (number of people with the disease) levels in an effort to evaluate the price-volume relationship and establish a reasonable market impact test. Including the size of the market as a factor would also allow the PMPRB to reassess the prices of patented medicines over time. Once a medicine is on the market, the patentee may seek regulatory approval from Health Canada to use the medicine in the treatment of other conditions, or the medicine might also be prescribed by physicians off-label (i.e. prescribed for the treatment of conditions for which the medicine has not received regulatory approval). Since patented medicines are protected from new entrants, their prices can remain unaffected from subsequent fluctuations in the size of the market into which they may be sold. As patentees are assumed to set their introductory prices at a profitable level to recoup initial investment, a growth in the market size should align and correct prices downwards to a comparable level. Failure to do so could suggest that the original price, for an expanded market, is now excessive.

*GDP in Canada and GDP per capita in Canada*

The GDP is a measure of a country's economic output. GDP growth measures how much the inflation-adjusted market value of the goods and services produced by an economy is increasing over time. Per capita GDP measures how much a country is producing relative to its population. Growth in Canadian GDP can be taken as an indicator of the country's ability to pay year-over-year, whereas per capita GDP is a proxy for buying power at the level of the individual. The introduction of GDP in Canada and GDP per capita in Canada as a price regulatory factor would provide the PMPRB with measures of ability to pay for medicines at the national and individual level. The inclusion of this factor would allow the PMPRB to assess the impact of a medicine's price on the finances of consumers and insurers. It could also enable the PMPRB to develop market impact tests for medicines that are likely to pose affordability challenges for insurers due to the market size for the medicine.

## 2. Update the schedule of countries used by the PMPRB for international price comparisons to be better aligned with the PMPRB's consumer protection mandate and median OECD prices

The PMPRB uses the publicly available list prices of patented medicines sold in the PMPRB7 to set maximum prices for the same patented medicines in Canada at introduction and in subsequent years. Depending on their price levels, the selection of countries can have a significant impact on the maximum prices for patented medicines in Canada.

This proposed amendment would reconsider the PMPRB7 to update the list of countries set out in the schedule to be better aligned with the PMPRB's consumer protection mandate, and Canada's wealth and status as a major market for medicines. The scope of countries considered for the revised schedule was the 35 OECD countries, as they share the same economic and social policies as Canada. Requiring patentees to report on prices in all 35 member countries was deemed unnecessary because (1) this would present a significant reporting burden; (2) some OECD countries are better aligned with Canada's domestic policy priorities and economic standing; and (3) it may be difficult to obtain price and sales information from some countries. Three criteria were used to select a subset of OECD countries to form the revised schedule.

First, the countries must have medicine pricing policies that are well aligned with the consumer protection mandate of the PMPRB, such as a country having national pricing containment measures to protect consumers from high medicine prices. For example, the United States does not satisfy this criterion.

Second, countries must possess reasonably comparable economic wealth as Canada, such as a country having a similar economic standing to Canada, as measured by GDP per capita. This is to ensure that prices correspond to Canada's ability to pay for medicines. For example, Canada's GDP per capita ranks eleventh among OECD countries, but prices for patented medicines are the third highest. The proposed schedule includes countries that have reasonably higher, similar and lower GDP per capita as Canada.

Third, countries are required to have a similar medicine market size characteristics as Canada, such as population, consumption, revenues and market entry of new products. This is to ensure that the resulting similar-sized markets produce a price level that is commensurate with Canada's share of global medicine sales.

Using these criteria, the proposed schedule lists Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, South Korea, Spain, Sweden and the United Kingdom (PMPRB12). Including a larger number of countries in the schedule would make price tests less sensitive to the influence of countries with

prices that are high or low, and reduce the impact where price and sales information is delayed or not available. For example, with only seven reference countries, delayed or missing price information from just two of the reference countries could impact the sample median by as much as 10%. Increasing the schedule to 12 countries would reduce this impact to just 2%. This slightly larger list would provide the PMPRB with a more balanced perspective of prevailing market prices and greater stability of the sample median without imposing significantly greater reporting requirements on patentees or administrative burden on the PMPRB.

### 3. Reduce reporting obligations for patented veterinary, over-the-counter and "generic" medicines

The Regulations currently only require patented veterinary and over-the-counter medicines (that do not contain a controlled substance or are not a radiopharmaceutical or biologic as per the *Food and Drugs Act* and the *Food and Drug Regulations*) to report price and sales information to the PMPRB on a complaints basis. Proposed amendments would further reduce reporting obligations for these medicines so that price, sales, and identity information would only be required on request by the PMPRB for all patented veterinary and over-the-counter medicines, including those that may contain a controlled substance, or are a radiopharmaceutical and/or a biologic. Amendments would also extend the same reduced reporting obligations to patented generic medicines (i.e. medicines approved by means of an ANDS). Patentees of generic medicines typically face greater competition, and the risk of excessive pricing due to market power is generally not cause for concern. These proposed amendments are intended to spare patentees unnecessary reporting regulatory burden for medicines that pose a lower risk of excessive pricing. It would also allow the PMPRB to focus its resources on medicines that pose a more substantive risk of excessive pricing.

### 4. Set out the patentee pricing information reporting requirements to enable the PMPRB to operationalize the new pricing factors

The current Regulations specify what information patentees must provide to the PMPRB in support of the current price regulatory factors. This includes information about the prices of patented medicines sold in Canada and other countries, patentees' revenues and R&D expenditures. Patentees would be required to report new information to the PMPRB to support the new pharmacoeconomic value and market size factors. Patentees would not be required to report on information related to GDP and GDP per capita, as this information would be obtained from Statistics Canada.

Information regarding pharmacoeconomic value: patentees would be required to provide the PMPRB with all published cost-utility analyses that express the value in terms of the cost per quality-adjusted life year (QALY). Cost-utility analyses are viewed by experts as the "gold standard" approach to considering the economic value of new medicines. The cost per QALY quantifies benefit by measuring lengthened life and/or improved quality of life. It is the most established measure of pharmacoeconomic value, as it enables comparisons across different types of medicines by using a common unit of measurement. This information reporting requirement would enable the PMPRB to consider the introduction of the concept of a maximum cost per QALY threshold in Canada.

In recognition of the significant expertise that can be necessary to prepare and validate cost-utility analyses, reporting would be limited to those that have been prepared by a publicly funded Canadian organization, such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or the Institut

national d'excellence en santé et services sociaux (INESSS). These organizations have dedicated expertise, and they generally conduct pharmacoeconomic analyses for medicines seeking to be reimbursed by public insurers. The PMPRB would consider these analyses in its evaluation of price excessiveness. It would not duplicate the work conducted by CADTH and INESSS as part of reimbursement processes.

Even though the new pharmacoeconomic value factor would only apply to sales of patented medicines made after the coming into force of the amended Regulations, the obligation to submit the most recently published cost-utility analysis would extend to all patented medicines, both those marketed as of the date of the amended Regulations coming into force and any new medicines offered for sale following the date of the coming into force. Cost-utility analyses are typically only prepared for a given medicine following certain trigger points in a medicine's life cycle (e.g. at time of initial market launch or following regulatory approval for use of the medicine in the treatment of a new condition). Although the most recent cost-utility analysis for an existing medicine could be several years old, it would still reflect the most recent and relevant information for the PMPRB to consider when applying the new factor of pharmacoeconomic value. Patentees would only be required to provide published analyses — there would be no obligation on the patentee to prepare a cost-utility analysis if one does not exist.

Information respecting market size: patentees would be required to provide the PMPRB with information on the estimated maximum use of the medicine in Canada, by quantity of the medicine sold in final dosage form, for each dosage form and strength that are expected to be sold. It is expected that patentees already construct this estimate as part of their development plans to introduce a new patented medicine to the Canadian market. Patentees compile this information in the development of business plans and for CADTH processes. Before going to market, patentees rely upon available statistics and information on the prevalence (number of people with a disease) in a given country and incidence (estimated number of new cases each year) to develop a sales forecast. They also take into account other factors such as competition to estimate the potential market share for their new medicine.

Patentees would also be required to provide the PMPRB with updated estimates that may occur, for example, when a medicine receives approval from Health Canada for use in the treatment of a new condition that expands the estimated market for the medicine. The new factor of market size would only apply to sales of patented medicines made after the coming into force of the amended Regulations. However, in view of the fact that it can take up to three years for the market for a new medicine to fully mature, patentees of medicines that are already on the market and were first offered for sale within three years prior to the amended Regulations coming into force or have received regulatory approval for use in the treatment of a new condition within this same three-year period would be required to provide information on the estimated maximum use of these medicines in Canada.

## 5. Require patentees to report price and revenues, net of all price adjustments

The Regulations currently require patentees to report information on price adjustments for the first point of sale only. Patentees are not required to report the significant price adjustments they may provide to third party insurers such as provincial insurers that provide reimbursement for the cost of a medicine sold to a patient. Provincial insurers are some of the biggest payers of patented medicines in Canada. Without this information, the PMPRB sets the non-excessive price maximum of a medicine on the basis of information that only includes some price adjustments. This amendment would require patentees to report price and revenue information that is net of any price or other adjustments, including discounts, rebates and free goods and services, to any party that pays for, or reimburses, the medicine. Although most adjustments are

likely to result in a price reduction, this amendment is intended to capture information on any adjustment including those resulting in a price increase. This information would be considered privileged as per section 87 of the *Patent Act* and would be considered by the Board when determining excessiveness.

With this information, the PMPRB would use the price that is net of any price adjustments to calculate the non-excessive price maximum. The PMPRB currently regulates the non-excessive price of a medicine based on the prices of other medicines in the same therapeutic class for sale in Canada. Since that price information does not include third-party price adjustments, the prices of comparator products that subsequently enter the market are often inflated (as the price ceilings for those medicines are determined in relation to an inflated list price of the existing medicine, rather than the actual price paid in Canada). As a result, the therapeutic class comparison tests yield price maximums that are higher than they would be if the actual price paid were available to the PMPRB. Compelling actual price information, inclusive of all price adjustments provided by the patentee, would allow the PMPRB to include rebates in the calculation of the average transaction price. It would also provide a mechanism for patentees to comply with the regime by calculating a true transaction price reflective of all rebates and discounts, direct and indirect.

## Regulatory and non-regulatory options considered

Status quo

The option of taking no action was considered and rejected on the grounds that the PMPRB's current regulatory framework lacks effective price regulatory factors and sufficient patentee price information reporting requirements. The current factors do not take into account all the aspects of excessiveness for new categories of medicines that have emerged since the creation of the PMPRB. The PMPRB's current patentee price information reporting requirements produce incomplete domestic pricing information and provide international price information from a number of countries with high patented medicine prices that are not equivalent to the Canadian market.

Non-regulatory modernization (updates to the PMPRB's *Compendium of Policies, Guidelines and Procedures*)

This option would be primarily limited to revised price tests that continue to rely completely on domestic and international price referencing methods. This option was fully explored, and included a stakeholder consultation by the PMPRB in 2016, but was rejected on the grounds that simply updating the guidelines does not address the underlying inadequacies of the existing Regulations. Regulatory reform is needed to obtain all price adjustment information and lessen the current dependence on international price testing through the addition of new factors. Under a modernized regulatory framework, the PMPRB would have a stronger basis from which to modernize its guidelines.

## Benefits and costs

The quantitative benefits from the cost-benefit statement relate to lower overall spending on patented medicines in Canada that is anticipated to result from lower prices. The quantified costs relate to (1) reduced industry revenues due to lower prices for patented medicines; (2) the net impact of new and reduced administrative industry reporting requirements; and (3) the costs to the Canadian government to ensure compliance with the proposed amendments.

The total quantified benefit of lower patented medicine prices is estimated at $21.3 billion (PV) over 10 years. The total quantified cost of this proposal, including all of the industry's lost revenues, is estimated at $8.6 billion (PV) over 10 years. Administrative costs to industry and the Government of Canada are anticipated to be approximately $62 million (PV) over 10 years. The total net benefits of the proposed amendments are estimated to be $12.7 billion (NPV) over 10 years, from 2019 to 2028. A discount rate of 7% was used in all PV calculations. The complete cost-benefit analysis is available upon request.

*Cost-benefit statement*

| **Quantified impacts** (*CAN$, 2017 price level/constant dollars*) | | | | |
|---|---|---|---|---|
| | **Base Year (Year 1)** | **Final Year (Year 10)** | **Total (PV)** | **Annualized Average** |
| **Benefits** | | | | |
| Lower drug expenditure | $219,993,857 | $2,782,694,694 | $8,567,004,599 | $1,219,745,515 |
| • New factors | $33,443,984 | $1,399,184,431 | $3,763,190,611 | $535,792,273 |
| • Updated schedule | $138,187,981 | $770,272,294 | $2,788,004,256 | $396,948,040 |
| • Third-party price adjustments | $48,361,892 | $613,237,969 | $2,015,809,732 | $287,005,201 |
| Health care system | $425,688,113 | $5,384,514,233 | $12,722,001,829 | $1,811,322,089 |
| **Total benefits** | $645,681,970 | $8,167,208,927 | $21,289,006,428 | $3,031,067,604 |
| **Costs** | | | | |
| Industry | | | $8,567,068,356 | $1,219,754,583 |
| • Loss revenues | $219,993,857 | $2,782,694,694 | $8,567,004,599 | $1,219,745,515 |
| • Administrative cost (includes regulatory burden reduction) | | | $34,717 | $4,924 |
| • Compliance cost | | | $29,106 | $4,144 |
| Government | $4,981,481 | $8,025,361 | $61,716,822 | $8,787,064 |
| • PMPRB program expenditure | $3,849,215 | $5,680,633 | $43,361,629 | $6,173,704 |
| • Special purpose allotment | $981,481 | $2,025,361 | $16,119,394 | $2,295,033 |
| • Accommodation requirements | $143,085 | $304,667 | $2,131,142 | $303,425 |
| • IT services | $7,700 | $14,700 | $104,657 | $14,900 |
| **Total costs (PV)** | | | $8,628,785,178 | $1,228,541,647 |

| | | |
|---|---|---|
| **Net benefits (NPV)** | $12,660,221,250 | $1,802,525,957 |
| Qualitative impacts | | |
| • Greater population health and increased savings to the health care system due to fewer acute care incidents. Lower prices could result in lower patient cost-related non-adherence to needed medicines (for example not filling prescriptions or skipping doses).<br>• Providing the opportunity to improve access to drugs and reallocate resources to other important areas of the health care system.<br>• Reduction in the burden placed on price negotiating bodies (e.g. the pan-Canadian Pharmaceutical Alliance) to ensure system affordability.<br>• Potential impact on wholesalers, distributors, pharmacies, and generic medicine manufacturers whose markups and prices are often expressed as a percentage of patented medicines prices. | | |

Costs

Patentee price information reporting requirements already exist under the current regulatory framework. For the most part, the types of information to be reported and the reporting frequency would remain unchanged. The increased administrative burden on the industry would be to report in relation to the new price regulatory factors. The proposal also includes the benefit of reduced administrative burden for certain types of medicines (patented over-the-counter, veterinary, and ANDS-approved medicines), but this reduction would not be sufficient to fully offset the new reporting requirements.

*Industry*

Industry costs would include the

- Reporting requirements on the new price regulatory factors. Patentees would ensure that the information be updated as new analyses are undertaken. Total administrative costs to report in relation to the new price regulatory factors are estimated to be $6,175 annually or $43,373 in PV over 10 years.
- Compliance cost to update reporting systems to include the proposed schedule of countries on which patentees must report pricing information every six months, and updating their domestic prices and net revenues to include all price adjustments. Patentees already have reporting systems in place for domestic and international prices — the proposal only modifies the type of information to be reported. Total compliance costs are estimated to be $4,144 annually or $29,106 in PV over 10 years.

*Administrative burden reduction*

The proposal removes the need for patented veterinary, over-the-counter, and generic drugs to file identity and price information with the PMPRB, unless that information is requested by the PMPRB. There are 96 medicine products (out of PMPRB's 1 359) that fall into these categories and are currently required to file information with the PMPRB. Given that the Federal Court of Appeal only recently clarified and upheld the PMPRB's jurisdiction over these medicines, the compliance for reporting of these medicines has not historically been considered by the PMPRB. Assuming full compliance, the administrative burden reduction is expected to be $8,656 (PV) over 10 years.

*Lost revenues to the medicine industry*

The PMPRB only regulates excessive patented medicine prices in Canada. Any price reduction and repayment of excess revenues that would occur as a result of this proposal would be pursuant to a voluntary compliance undertaking (VCU) by the patentee to comply with the new maximum compliant price levels, or pursuant to a Board Order made following a public hearing before the Board where a Board Panel determines that the medicine has been sold at an excessive price. It is estimated that this proposal will result in reduced industry revenues of approximately $8.6 billion (PV) over 10 years, due to reduced thresholds for maximum non-excessive prices in Canada. For the purpose of this cost-benefit analysis (CBA), national treatment of revenue was given to all patented medicine manufacturers in Canada, despite the fact that 90% of the companies that report to the PMPRB are multinational enterprises (MNEs).

*Government of Canada*

*Increasing the PMPRB's capacity*

Costs to Government would include funds for the PMPRB to hire additional staff to support the expected increase in enforcement-related activities, and to administer the new price regulatory factors. The base (2018–19), second (2019–20), third (2020–21), and fourth years (2021–22) would be anticipated to cost $3.8 million, $5.7 million, $6.7 million, and $7.7 million, respectively. From the fifth year onwards, it is anticipated that costs to Government would be $5.7 million/year to maintain the PMPRB's increased capacity.

*Increasing special purpose allotment funding*

With the proposed new Regulations in place, patentees might be less willing to offer voluntary compliance undertakings and instead press for formal and potentially prolonged hearings. The PMPRB would require additional funding for its special purpose allotment (SPA) to cover the costs of outside legal counsel and expert witnesses. Patentees might also more frequently challenge decisions made under the new regime in the Federal Court. The base (2018–19), second (2019–20), third (2020–21), and fourth years (2021–22) would be anticipated to cost $1.0 million, $1.8 million, $2.8 million, and $3.8 million, respectively. From the fifth year onwards, it is anticipated that costs to Government would be $2.0 million/year to maintain the PMPRB's increased SPA funding.

*Offsetting costs to Public Service and Procurement Canada and Shared Services Canada*

Increasing the PMPRB's staffing levels would also increase accommodation and information technology (IT) costs. Combined, the base (2018–19), second (2019–20), third (2020–21), and fourth years (2021–22) would be anticipated to cost $151,000, $305,000, $328,000, and $331,000, respectively. From the fifth year onwards, it would be anticipated that costs to Government would be $319,000/year to offset Public Service and Procurement Canada's accommodation costs and Shared Services Canada's IT services costs.

The total cost to the Government of Canada would be anticipated at $61.7 million in net present value over 10 years.

Benefits

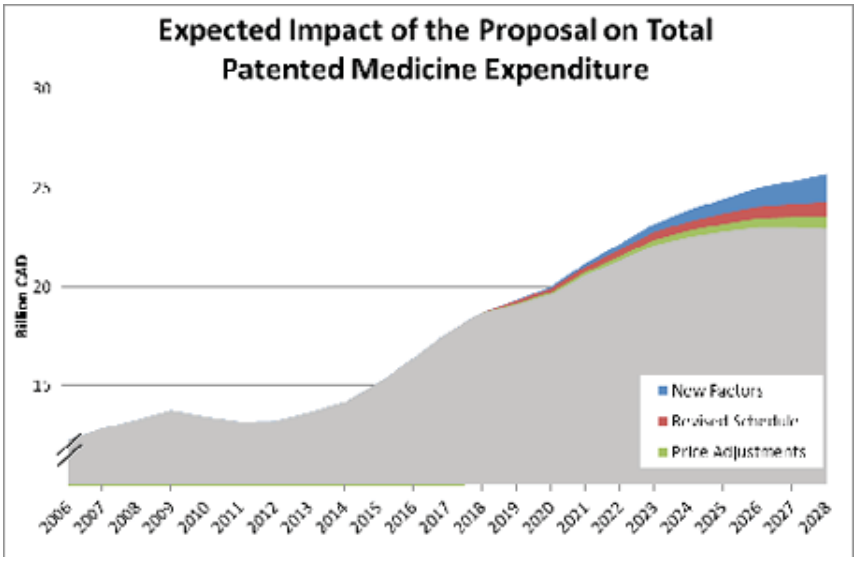
Benefits were calculated based on the expected reduction in the level of public risk of excessively priced patented medicines in Canada.

Anticipated quantitative benefits were calculated on the basis of reduced overall spending on patented medicines. The projected baseline of future spending (2017–2028) was calculated using current growth trends and anticipated launches from the current medicine pipeline. It also includes the expected loss of patent protection of medicines that are currently under the PMPRB's jurisdiction. The total net benefits arising from the proposed amendments are estimated to be $25.1 billion dollars (NPV) over 10 years.

## Lower patented medicine expenditure

The proposed amendments are expected to lower patented medicine expenditure by an estimated $8.6 billion (PV) over 10 years.

The introduction of the new price regulatory factors would be expected to have the biggest impact on patented medicine expenditure ($3.8 billion), followed by the revised schedule ($2.8 billion) and the reporting of price and sales adjustment with third parties ($2.0 billion).




*Healthcare system benefits*

Without the proposed amendments, it is estimated that public health care systems from across Canada will spend an additional $3.9 billion (PV) for the same quantity of patented medicine. This represents a significant opportunity cost for the Canadian public health care system, as these funds could have been used in other areas of the health care system to better the health of Canadians. Given the large ripple effects on health and the economy for every dollar spent in public health, (see footnote 1) the size of this opportunity cost in Canada is quite substantial. The total opportunity cost to the health care system of paying for excessively priced medicines was estimated to be $12.7 billion dollars (PV) over 10 years.

*Sensitivity analysis summary*

A sensitivity analysis was performed in relation to two variables that could greatly affect the estimated impact of the proposal. The first variable relates to the PMPRB implementation of the proposal and the other to the projected growth rate in patented medicine expenditure. The baseline analysis was conducted on an assumption that the PMPRB continues to apply price test methods that are similar to those currently in place. This assumption is necessary since any changes to the guidelines are fully within the control of the PMPRB. For example, the PMPRB currently uses the median PMPRB7 price to test new medicines against prices in other countries. The baseline assumes that the median price test would also be applied to the new

PMPRB12. The sensitivity analysis of this variable examined possible alternate approaches to the existing price regulatory factors as well as possible approaches to implementation of the proposed new factors in the guidelines.

The second variable relates to the growth of expenditures in patented medicines. If growth in patented medicine expenditure is higher than anticipated, the benefit measured in dollars, calculated from a percent reduction due to lower patented medicine prices, will be higher than anticipated. Likewise, if growth in expenditure is lower than anticipated, then the overall benefit will also be lower. Growth in the patented medicine industry is difficult to predict, and the emergence of new types of patented medicines, such as biologics, introduces new uncertainties into modelling efforts.

The sensitivity analysis demonstrates that total patented medicine expenditure could be lowered from a minimum of $6.4 billion dollars (PV) after 10 years to a maximum of $24.9 billion dollars (PV) after 10 years. The minimum sensitivity analysis impact represents the lowest projected patented medicine sales growth coupled with the least aggressive reforms to the PMPRB guidelines. The maximum sensitivity analysis impact represents the highest projected patented medicine sales coupled with the most aggressive reforms to the PMPRB guidelines. The current CBA estimates the baseline cumulative expenditure after 10 years to be $8.6 billion dollars (PV). (see footnote 2)

*Distributional analysis summary*

The vast majority of patented medicine manufacturers are located in Ontario, Quebec, British Columbia, and Alberta. These four provinces constitute 98% of all companies that would be affected by the proposed amendments.

All — public, private, and out-of-pocket — payers of patented medicines from across the country will benefit from lower prices.

Usage by age and gender: According to Statistics Canada's report "Prescription medication use by Canadians aged 6 to 79," prescription medicine use rose with age from 12% among 6- to 14-year-olds to 83% among 65- to 79-year-olds. Prescription medicine use was also associated with the presence of physical and mental health conditions. The percentage of Canadians taking prescription medicines did not differ by household income. Females were generally more likely than males to report taking prescription medications (47% versus 34%). However, at ages 6 to 14, a higher percentage of boys, rather than girls, used prescription medications, and at ages 65 to 79, the prevalence of prescription drug use was similar for men and women. Prescription drug use intensity — the number of different medications taken — was strongly associated with age. The percentage taking more than one medication rose from 3% at ages 6 to 14 to 70% at ages 65 to 79.

## "One-for-One" Rule

The estimated added regulatory burden to patentees was calculated to be approximately $43,373, with an estimated reduction in regulatory burden of $8,656, for a total of $34,717 (PV over 10 years). This calculation includes the upfront cost of providing the PMPRB with cost-utility and market size analyses for medicines currently under the jurisdiction of the PMPRB, the ongoing costs of updating these analyses and providing the PMPRB cost-utility analyses and market size estimates for all new patented medicines that enter the market, as well as further reducing the current reporting requirements for patented veterinary, over-the-counter medicines, and adding generic medicines to those same reduced reporting obligations. The proposal is considered an "IN" under the "One-for-One" Rule and has an estimated impact of $3,062.

| *Current initiative is an:* | *"IN" ("One-for-One" Rule)* | | |
|---|---|---|---|
| | **Values to Report in Regulatory Impact Analysis Statement** | **Rounding** | **Unit of Measure** |
| Annualized administrative costs (constant $2012) | $3,062 | 0 digits | Constant 2012 dollars, present value base year: 2012 |
| Annualized administrative costs per business ($2012) | $40 | 0 digits | Constant 2012 dollars, present value base year: 2012 |

## Small business lens

The small business lens does not apply to the proposed amendments, as only medicine manufacturers that have a patented medicine for sale in Canada would be affected by the proposed amendments. Among the 77 companies reporting to the PMPRB, none were identified as satisfying the small business definition. In general, patented medicines are sold by multinational enterprises or their subsidiaries.

## Consultation

The consultation period for prepublication in the *Canada Gazette*, Part I, of the regulatory proposal will be 75 days.

This consultation builds on an initial consultation on the regulatory proposal. On May 16, 2017, the Honourable Jane Philpott, former federal Minister of Health, announced the launch of the consultation on the proposed amendments to the *Patented Medicines Regulations.* A consultation document entitled "Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations" was posted on Health Canada's website as well as the Government of Canada's Consulting with Canadians website. The consultation was promoted through a news release and an email notification that was distributed widely to stakeholders. In addition, to comply with subsection 101(2) of the *Patent Act*, Minister Philpott wrote each of her counterparts in the provinces and territories, inviting comments on the proposed regulatory amendments. Written submissions from all stakeholders and interested parties were accepted until June 28, 2017. During the consultation period, Health Canada hosted nine engagement sessions with external stakeholders, including representatives from public and private insurers, patient organizations, the medicine industry, the health professions and academia.

Insurers (public and private) were supportive overall, noting that pharmacoeconomic value and market size are very relevant to the determination of price excessiveness. There was no consensus around GDP as a factor. Private insurers suggested that the factors account for considerations relevant to employers, such as the impact of the medicine on productivity, absenteeism, and disability claims. Insurers supported the revised schedule of countries. While in favour of reducing regulatory burden for patented generic medicines, insurers suggested that the PMPRB still request price and sales information for patented generics at risk of higher prices. Finally, insurers were supportive of the amendment to provide the PMPRB with price adjustment information, on the condition that this information remain confidential to the PMPRB.

Patient organizations noted that the high prices of new patented medicines pose a financial barrier to access for Canadians and asked that the Regulations ensure that patient access to medicines is a primary concern. Patient organizations suggested that there be enough flexibility in the Regulations to allow the PMPRB to go beyond the cost per QALY to take patient preferences into account and to consider special circumstances such as medicines for rare diseases. In addition, organizations asked that the use of price adjustment information in regulating prices not compromise the bargaining position of insurers.

Representatives of the brand name medicine industry suggested that proposed amendments would add significant complexity and uncertainty for patented medicines to reach the market in Canada. A number of representatives suggested that the proposed economic-based factors go beyond the mandate of the PMPRB and are potentially duplicative of CADTH's assessment. They expressed concern around the additional regulatory burden of providing international pharmacoeconomic and pricing information. A common suggestion was that the United States should remain in the schedule of countries. It was recommended that the Regulations allow for a risk-based approach and that regular reporting requirements should be removed for lower-risk products. It was not clear to the industry how the PMPRB plans to use and protect confidential price adjustment information; however, it was suggested that providing this information to the PMPRB would risk lower price adjustments for insurers in Canada.

Generic medicine industry representatives supported the proposal to remove the requirement for patented generic manufacturers to regularly report information about the identity and price of these medicines, as they pose a low risk of abusing market power and are subject to price regulation by the provinces and territories. They recommended this amendment be extended to include other complex forms of generics that do not receive a Declaration of Equivalence from Health Canada, such as biosimilars and generics with complex ingredients and formulations.

The consumer health products industry acknowledged that the over-the-counter products (OTCs) it produces are already exempt from reporting regularly. Representatives recommended that all self-care products be exempt entirely from the patented medicine framework; however, it is beyond the scope of the Regulations to change the PMPRB's jurisdiction over patented medicines.

Representatives from physicians' and nurses' associations supported economics-based factors to assess the value of a medicine, the revised schedule and requiring information on confidential rebates in Canada. Nurses' associations were not supportive of exempting patented generics from systematic reporting requirements. Pharmacists supported assessing a medicine based on its value, but noted that pharmacoeconomic value should consider benefits and costs beyond a QALY. They noted that the schedule of comparator countries should be revised based on the availability of products in each country and asked that the amendment pertaining to confidential price adjustments not compromise the price adjustments negotiated by public insurers.

Academics supported the proposed pharmacoeconomic value factor and cost per QALY information requirement. Some academics supported using GDP to set an upper bound on prices and suggested the use of per capita GDP. Academics were less convinced that market size information would be useful without more information on the R&D costs of a medicine. Most agreed with revising the schedule and removing countries that do not have consumer protections in place for excessive prices. Academics were generally in favour of allowing the PMPRB to collect information on adjustments in price, but they suggested it be broadened to include all types of transfers from patentees that impact prices, including pay-for-performance agreements, and cautioned against using rebate information when making international comparisons.

The responses related to the Regulations have been taken into consideration in the development of this proposal for prepublication in the *Canada Gazette*, Part I, and the Regulatory Impact Analysis Statement. In particular,

- The economics-based price regulatory factors in the proposed amendments have remained broad in order to provide the PMPRB with the flexibility to consider other measures beyond the cost per QALY where relevant, and to enable the PMPRB to develop appropriate measures using market size and GDP. Based on feedback received, GDP per capita has been added to the GDP factor.
- The information reporting requirements for patentees have been revised to minimize the regulatory burden while providing the PMPRB with sufficient information to protect Canadians from excessive prices. The proposed amendments do not require cost-utility analyses (CUAs) from countries other than Canada to be reported.
- Further analysis has been provided on the proposed schedule; an estimate of the impacts on patented medicine expenditures is provided in the cost-benefit analysis.
- Consideration was given to the removal of systematic information reporting requirements for patentees for other low-risk products beyond patented generic medicines. It is proposed that regular reporting requirements be removed for all patented over-the-counter medicines, including radiopharmaceuticals and biologics authorized for sale under the *Food and Drug Regulations* as well as those containing controlled substances. While other products such as biosimilars and other patented generic medicines that are not authorized for sale by way of an ANDS were considered, these products and their risk of excessive pricing could not be adequately defined.
- It is proposed that the new information reporting requirements in the Regulations capture all price adjustments that would serve to lower (e.g. discounts, rebates, free goods, free services) or raise (e.g. payment for performance) the price of a medicine.

### Regulatory cooperation

This proposal would update the schedule of countries used by the PMPRB for international price comparisons to be better aligned with the PMPRB's consumer protection mandate and median OECD prices. This international alignment would contribute to lowering medicine prices for Canadians.

### Rationale

Unlike most international health systems, Canada's health system does not have a single payer for medicines. Canadian expenditure on prescription medicines is split between public insurers (43%), private insurers (35%) and Canadians paying out-of-pocket (22%).

Modernization of the PMPRB's regulatory framework would benefit all those who pay for medicines in Canada through a higher standard of consumer protection. Canada's public and private insurers would benefit from lower maximum prices so their price negotiations achieve more than simply prices that match those in other countries. The amendments would help the PMPRB to achieve Canadian maximum prices closer to international norms. This would allow public and private insurers to negotiate with sellers on a more equal footing with health authorities in other countries. Employer-sponsored health insurance plans are anticipated to benefit from lower premiums and reduced risk of becoming untenable due to high-cost medicines. Uninsured Canadians who pay out-of-pocket for their medicines rely most heavily on the consumer protection mandate of the PMPRB, and they would benefit from lower prices for their patented medicines.

This proposal is anticipated to result in an estimated total benefit to Canadians of $8.6 billion in net present value (NPV) over 10 years following implementation.

### Implementation, enforcement and service standards

The proposed Regulations would come into force on January 1, 2019. This would allow patentees time to prepare for implementation of the new price regulatory factors and information reporting requirements on prices. January 1, 2019, was the date chosen to align the implementation with the PMPRB's reporting periods of January 1 and July 1. Once the amended Regulations are published in the *Canada Gazette*, Part II, responsibility for implementation, enforcement and service standards would be passed to the PMPRB. This is anticipated to include the finalization of a PMPRB-led stakeholder consultation on a revised *Compendium of Policies, Guidelines and Procedures* that will be used to reach an understanding of how the revised framework would be embodied in the form of specific price tests and qualifying information to be reported by patentees.

The new factors may only be considered in relation to sales that occur after the coming into force of the proposed amendments. However, the reporting requirements in the amended Regulations would be applied to new and existing patented medicines alike. Patentees of existing medicines would have 30 days after the coming into force to provide the cost-utility analysis (if available) and estimated market use information (if applicable). Price information for the countries in the revised schedule and domestic price and revenue information that takes into account price adjustments would first be required to be reported within 30 days after the end of the reporting period in which the proposed amendments came into force (i.e. within 30 days after June 30, 2019).

### Contact

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## PROPOSED REGULATORY TEXT

Notice is given that the Governor in Council, pursuant to subsection 101(1) (see footnote a) of the *Patent Act* (see footnote b), proposes to make the annexed *Regulations Amending the Patented Medicines Regulations*.

Interested persons may make representations concerning the proposed Regulations within 75 days after the date of publication of this notice. All such representations must cite the *Canada Gazette*, Part I, and the date of publication of this notice, and be addressed to Karen Reynolds, Executive Director, Office of

Pharmaceuticals Management Strategies, Strategic Policy Branch, Health Canada, 10th Floor, Brooke Claxton Building, 70 Colombine Driveway, Tunney's Pasture, Ottawa, Ontario K1A 0K9 (tel.: 613-957-1692; email: PMR-Consultations-RMB@hc-sc.gc.ca (mailto:PMR-Consultations-RMB%40hc-sc.gc.ca)).

Ottawa, November 23, 2017

Jurica Čapkun
Assistant Clerk of the Privy Council

# Regulations Amending the Patented Medicines Regulations

## Amendments

**1 Section 3 of the *Patented Medicines Regulations*** (see footnote 3) **is amended by adding the following after subsection (3):**

**(3.1)** Despite subsection (3), in each of the following cases, the information referred to in subsection (1) must be provided to the Board within 30 days after the day on which the Board sends a request for the patentee to provide that information:

**(a)** the medicine is not a *prescription drug* as defined in section A.01.010 of the *Food and Drug Regulations*;

**(b)** the medicine contains a *controlled substance* as defined in subsection 2(1) of the *Controlled Drugs and Substances Act*, the sale or provision of which does not require a prescription under that Act;

**(c)** a notice of compliance has been issued in respect of the medicine on the basis of information and material contained in a submission filed under section C.08.002.1 of the *Food and Drug Regulations*; or

**(d)** the medicine is for veterinary use.

**2 (1) The portion of subsection 4(2) of the Regulations before paragraph (a) is replaced by the following:**

**(2)** The information referred to in subsection (1) must be provided

**(2) Subsection 4(3) of the Regulations is replaced by the following:**

**(3)** Despite subsection (2), in each of the following cases, the information referred to in subsection (1), for each six-month period beginning on January 1 and July 1 of each year, must be provided to the Board within 30 days after the day on which the Board sends a request for the patentee to provide that information and, during the two years following the request, within 30 days after the end of each six-month period:

**(a)** the medicine is not a *prescription drug* as defined in section A.01.010 of the *Food and Drug Regulations*;

**(b)** the medicine contains a *controlled substance* as defined in subsection 2(1) of the *Controlled Drugs and Substances Act*, the sale or provision of which does not require a prescription under that Act;

**(c)** a notice of compliance has been issued in respect of the medicine on the basis of information and material contained in a submission filed under section C.08.002.1 of the *Food and Drug*

*Regulations*; or

**(d)** the medicine is for veterinary use.

**(3) Paragraphs 4(4)(a) and (b) of the Regulations are replaced by the following:**

**(a)** in calculating the average price per package of a medicine, the actual price obtained by the patentee must be used, taking into account any adjustments that are made by the patentee or any party that directly or indirectly purchases or reimburses for the purchase of the medicine and any reduction given to any party in the form of free goods, free services, gifts or any other benefit of a like nature; and

**(b)** in calculating the net revenue from sales of each dosage form, strength and package size in which the medicine was sold in final dosage form, the actual revenue obtained by the patentee must be used, taking into account any adjustments that are made by the patentee or any party that directly or indirectly purchases or reimburses for the purchase of the medicine and any reduction given to any party in the form of free goods, free services, gifts or any other benefit of a like nature.

**3 The Regulations are amended by adding the following after section 4:**

**4.1 (1)** For the purposes of paragraphs 80(1)(d) and (2)(d) of the Act, the information to be provided respecting the factor referred to in paragraph 4.4(a) is every cost-utility analysis prepared by a publicly funded Canadian organization, if published, for which the outcomes are expressed as the cost per quality-adjusted life year for each indication that is the subject of the analysis.

**(2)** The information referred to in subsection (1) must be provided

**(a)** if the information is published when the medicine is first offered for sale in Canada, within 30 days after the day on which the medicine is first offered for sale in Canada; and

**(b)** if the information is not published when the medicine is first offered for sale in Canada, within 30 days after the day on which it is published.

**(3)** Despite subsection (2), in the case of a medicine that is offered for sale in Canada before January 1, 2019, the information referred to in subsection (1) must be provided

**(a)** if the information is published before January 1, 2019, by January 30, 2019; and

**(b)** if the information is not published before January 1, 2019, within 30 days after the day on which it is published.

**(4)** If any other analysis as described in subsection (1) is published after those referred to in subsection (1) were provided, it must be provided within 30 days after the day on which it is published.

**4.2 (1)** For the purposes of paragraphs 80(1)(d) and (2)(d) of the Act, the information to be provided respecting the factor referred to in paragraph 4.4(b) is the estimated maximum use of the medicine in Canada, by quantity of the medicine in final dosage form, for each dosage form and strength that are expected to be sold.

**(2)** The information referred to in subsection (1) must be provided within 30 days after the day on which the medicine is first offered for sale in Canada.

**(3)** Despite subsection (2), in the case of a medicine that is offered for sale in Canada before January 1, 2019, the most recent version of the information referred to in subsection (1) must be provided

**(a)** if the medicine is first offered for sale in Canada during the period beginning on January 1, 2016 and ending on December 31, 2018, by January 30, 2019; and

**(b)** if the information referred to in subsection (1) in respect of the medicine is not required to be provided under paragraph (a), but the information is updated

**(i)** during the period beginning on January 1, 2016 and ending on December 31, 2018, by January 30, 2019; or

**(ii)** after December 31, 2018, within 30 days after the day on which it is updated.

**(4)** The information provided under this section must be up to date and any modification of that information must be provided within 30 days after the day on which the modification is made.

**4.3 (1)** Despite subsections 4.1(2) and (3) and 4.2(2) and (3), in each of the following cases, the information referred to in subsections 4.1(1) and 4.2(1) must be provided to the Board within 30 days after the day on which the Board sends a request for the patentee to provide that information:

**(a)** the medicine is not a ***prescription drug*** as defined in section A.01.010 of the *Food and Drug Regulations*;

**(b)** the medicine contains a ***controlled substance*** as defined in subsection 2(1) of the *Controlled Drugs and Substances Act*, the sale or provision of which does not require a prescription under that Act;

**(c)** a notice of compliance has been issued in respect of the medicine on the basis of information and material contained in a submission filed under section C.08.002.1 of the *Food and Drug Regulations*; or

**(d)** the medicine is for veterinary use.

**(2)** The requirements of subsections 4.1(4) and 4.2(4) apply in respect of the information provided under subsection (1).

### Other Factors to be Considered — Excessive Prices

**4.4** For the purposes of paragraph 85(1)(e) of the Act, the other factors that the Board must take into consideration to determine whether a medicine that is sold in any market in Canada after December 31, 2018 is being or has been sold at an excessive price are the following:

**(a)** the pharmacoeconomic value in Canada of the medicine and that of other medicines in the same therapeutic class;

**(b)** the size of the market for the medicine in Canada and in countries other than Canada; and

**(c)** the gross domestic product in Canada and the gross domestic product per capita in Canada.

4 **The schedule to the Regulations is replaced by the schedule set out in the schedule to these Regulations.**

### Coming into Force

**5 These Regulations come into force on January 1, 2019.**

## SCHEDULE

(Section 4)

## SCHEDULE

(Subparagraph 4(1)(f)(iii))

Australia
*Australie*

Belgium
*Belgique*

France
*France*

Germany
*Allemagne*

Italy
*Italie*

Japan
*Japon*

Netherlands
*Pays-Bas*

Norway
*Norvège*

Republic of Korea
*République de Corée*

Spain
*Espagne*

Sweden
*Suède*

United Kingdom
*Royaume-Uni*

[48-1-o]

Footnote 1

Reeves et al. “Does investment in the health sector promote or inhibit economic growth?” *Globalization and Health* (2013) 9:43.

Footnote 2
As per TBS guidelines, the discount rate used to calculate the net present value was 7%.

Footnote 3
SOR/94-688; SOR/2008-70, s.1

Footnote a
S.C. 2017, c. 6, s. 57

Footnote b
R.S., c. P-4

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# Government of Canada activities and initiatives

**#YourBudget2018 – Advancement**

(https://www.budget.gc.ca/2018/docs/themes/advancement-advancement-en.html?utm_source=CanCa&utm_medium=Activities_e&utm_content=Advancement&utm_campaign=CAbdgt18)
Advancing our shared values

**#YourBudget2018 – Reconciliation**

(https://www.budget.gc.ca/2018/docs/themes/reconciliation-reconciliation-en.html?utm_source=CanCa&utm_medium=%20Activities_e&utm_content=Reconciliation&utm_campaign=CAbdgt18)
Advancing reconciliation with Indigenous Peoples

**#YourBudget2018 – Progress**

(https://www.budget.gc.ca/2018/docs/themes/progress-progres-en.html?utm_source=CanCa&utm_medium=Activities_e&utm_content=Progress&utm_campaign=CAbdgt18)
Supporting Canada's researchers to build a more innovative economy

# Appendix 5.2: PMPRB Guidelines Scoping Paper

Patented Medicine Prices Review Board

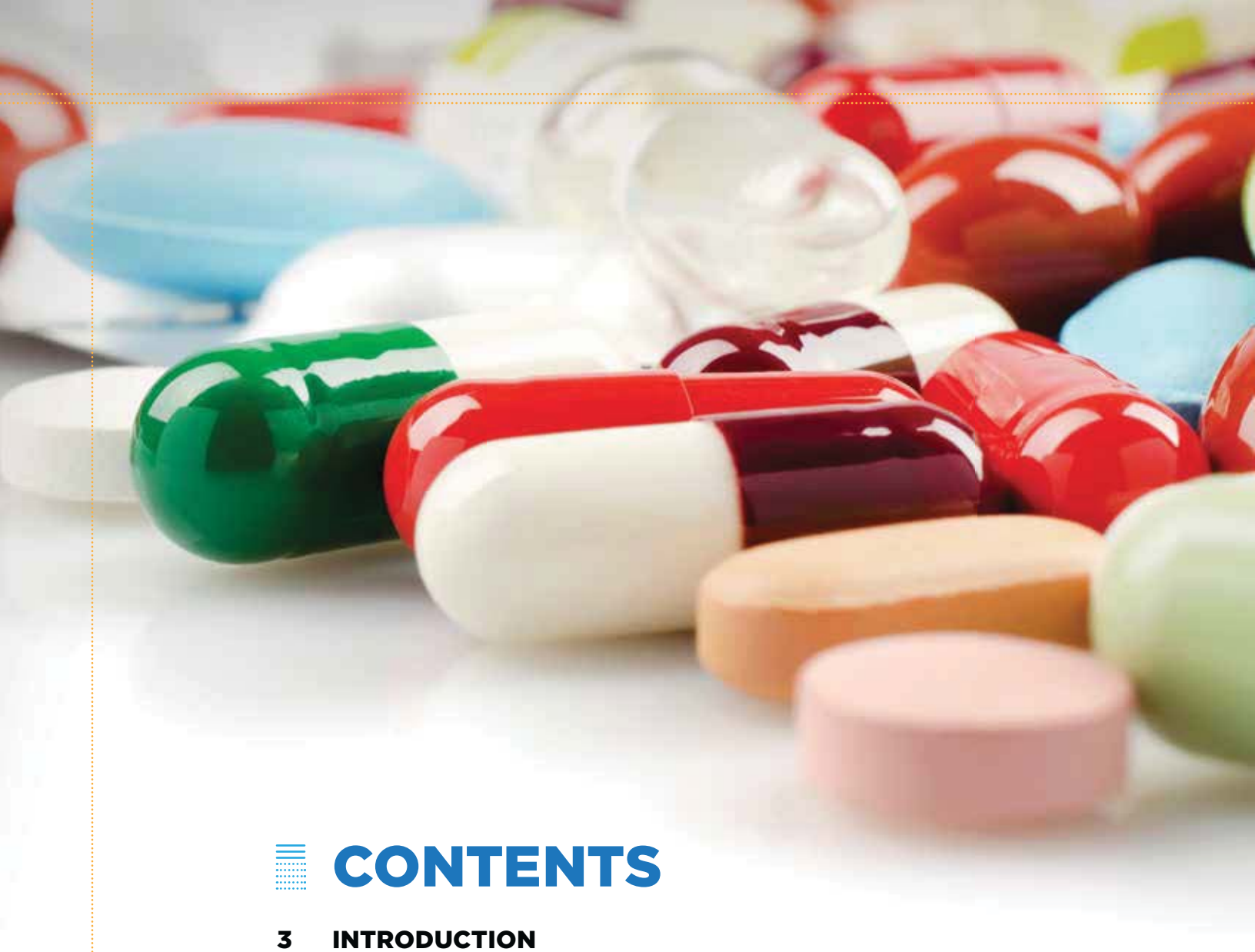
Conseil d'examen du prix des médicaments brevetés

# PMPRB GUIDELINES SCOPING PAPER

## High Level Overview of Potential New Framework

**CGI CONSULTATION PHASE**

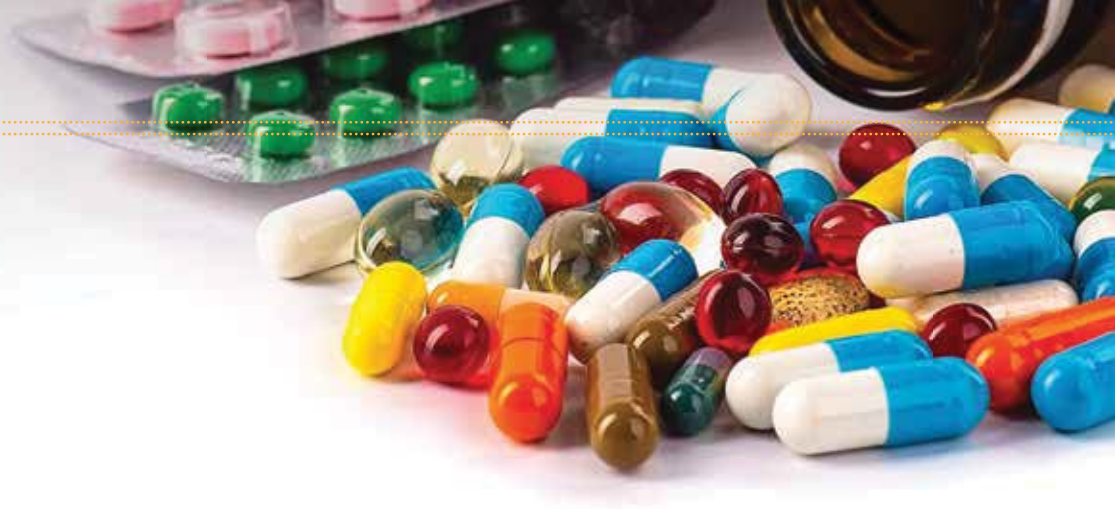
Canada



# CONTENTS

# INTRODUCTION

This scoping paper is intended to be read in conjunction with proposed amendments to the *Patented Medicines Regulations* ("Regulations"), and accompanying Regulatory Impact Analysis Statement (RIAS), which were pre-published in the December 2nd, 2017 issue of the Canada Gazette, Part I. Its purpose is to provide stakeholders and interested members of the public with an outline of the PMPRB's preliminary thoughts on how best to operationalize the proposed changes to the Regulations, through non-binding Guidelines as contemplated by s.96 of the *Patent Act*, within the context of the existing and proposed legislation and the PMPRB's ongoing efforts at reform. It is hoped that this document will serve as a catalyst for a more informed, focussed and productive consultation process on framework modernization, with a view to having new Guidelines in place by early 2019. This document is not to be viewed as a definitive interpretation of the current or proposed legislation or of the RIAS for the proposed amendments by the PMPRB, is not the Government's expression of policy intent or an official part of the Canada Gazette I (CGI) consultation, and is not intended to bind the PMPRB or the Government in the application and interpretation of legislation. The PMPRB will officially consult on a revised set of proposed Guidelines in the spring of 2018.

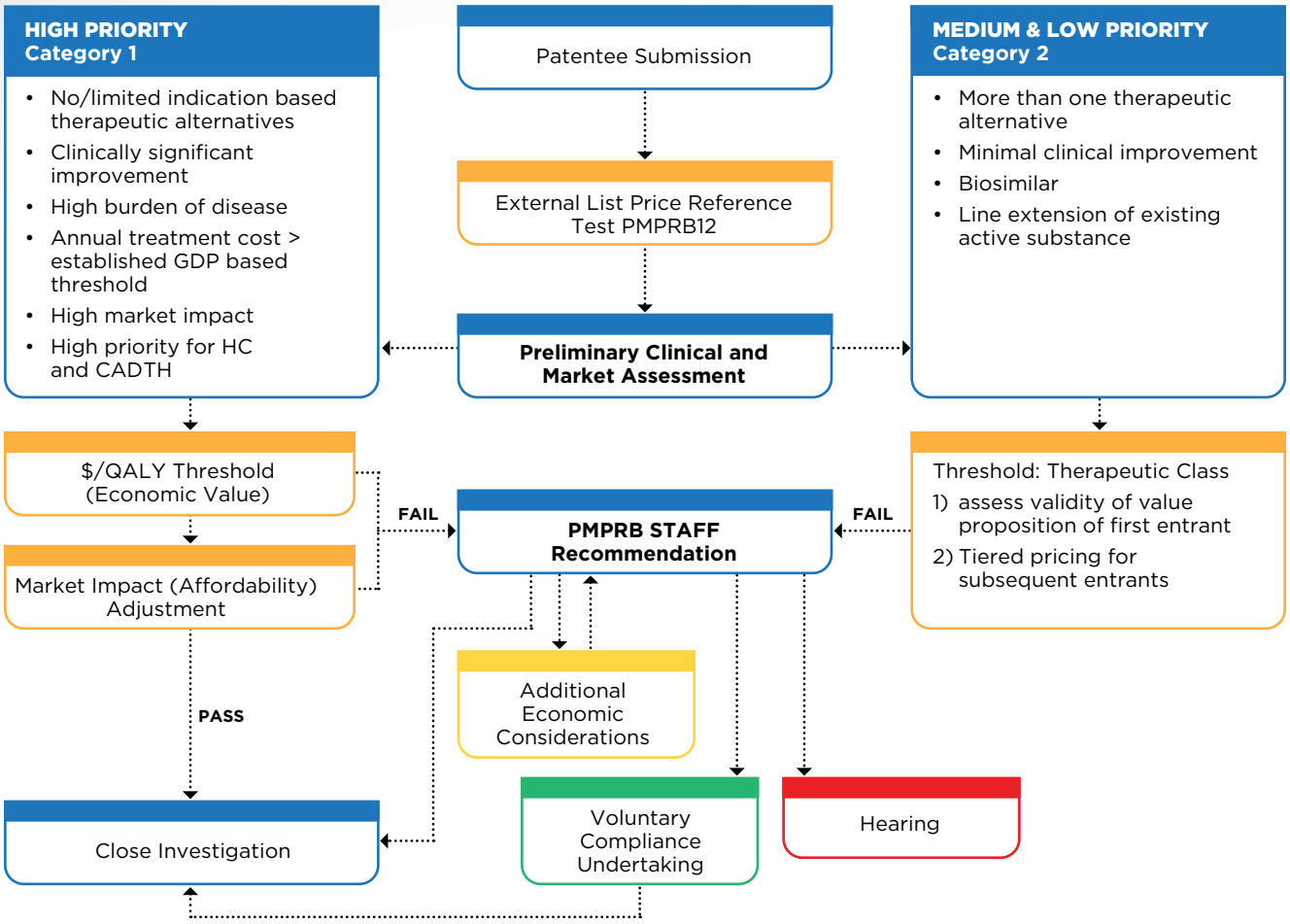


# THE NEW FRAMEWORK

As an expert economic regulatory body, the PMPRB must ensure that its new framework is grounded in sound and prevailing economic theory. In conceiving the mechanics of that framework, the PMPRB was mindful of the Minister of Health's stated policy rationale for the proposed regulatory amendments and of the overarching purpose of the current and proposed legislation. The PMPRB also sought to give effect to areas of stakeholder agreement that emerged from the recent Guidelines modernization consultation. Accordingly, to the extent possible, the framework envisaged by the PMPRB employs economically-derived, bright line tests to yield meaningful ceiling prices that are foreseeable to patentees. As before, the new Guidelines are proffered as rules of general application which serve as a mechanism for determining a rough estimate of where the line between potential non-excessive prices and potential excessive prices should be drawn by PMPRB staff. The objective of the Guidelines is to enable the calculation of a national ceiling price above which it would be unreasonable for any consumer in Canada to pay, not an ideal price for each payer based on their individual ability and willingness to pay.

While the details of the framework remain to be worked out through consultation, its basic structure can be described as a risk-based approach to pricing review that is broken down into five main parts, as illustrated in the following schematic and discussed in more detail below.

## PROPOSED PRICE REVIEW SCHEMATIC*




*For discussion purposes only, not intended to bind or limit the PMPRB or the Government in the application and interpretation of legislation

## Part I: Interim international price reference test

At introduction, all new drugs would first be subject to an interim price test based on the list price of a new drug in Canada against the list price in the proposed PMPRB12 basket of countries. Domestic and international list prices in today's environment of confidential discounts and rebates represent the starting point of a price negotiation rather than a true reflection of actual price paid in the market place. In this context, the PMPRB would look at how the proposed price in Canada compares to public list prices in other markets. If the price in Canada exceeds the median of the PMPRB12, it would be considered potentially excessive.

## Part II: Screening

The second part of the framework consists of a screening phase which would classify new patented drugs as either high or low priority based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans). At this stage in the process, the PMPRB would consider whether the drug is first in class, has few or no therapeutic alternatives, provides significant therapeutic improvement over existing treatment options, is indicated for a condition that has a high prevalence in Canada, is a high cost drug (i.e. an average annual cost higher than a GDP-based threshold) or is classified as a high priority drug by other agencies/regulators in the health care system (such as the Canadian Agency for Drugs and Technologies in Health (CADTH) or Health Canada) because of unmet medical need. Drugs that appear to be high priority based on these screening factors would be subject to automatic investigation and a comprehensive review to determine whether their price is potentially excessive.

## Part III: High priority drugs

Once a drug is assessed as high priority, the third part of the new framework would see the PMPRB apply a two-part test for evaluating potential excessivity[1].

The first part of the test would assess the incremental cost per quality-adjusted life year (QALY) of the drug, as determined by CADTH's health technology assessment process, against an explicit cost effectiveness threshold. The threshold would be based on the opportunity cost associated with displacing the least cost effective health technology in the Canadian health system, otherwise understood as the marginal cost of a QALY, as calculated by expert health economists and revised periodically to reflect changing market conditions. Drugs that prolong life or provide significant QALY gains could be subject to a more generous threshold, as Canadian payers have demonstrated a higher willingness to pay for these types of drugs.

The second part of the test would assess whether a drug that meets the cost effectiveness threshold should have its price further adjusted because of its expected impact on payers within the first three to five years from launch (assuming appropriate clinical utilization and no rationing of care). This test would consider the anticipated market size of the new drug against GDP growth, with the latter serving as a rough proxy for how much Canadian consumers can afford to pay for the new patented drugs that come to market on an annual basis. The test could also be used to allow a price adjustment upward in instances where a drug has a very high opportunity cost but very small market impact due to the extreme rarity of the condition it is indicated to treat.

[1] The test addresses current factors that the PMPRB must consider under s.85 of the *Patent Act* as well as the new factors that are identified in the proposed amendments to the Regulations published on December 2, 2017.

If the price fails this two-part test, the patentee would be provided with an opportunity to explain why the price of its drug is not excessive having regard to the cost of making or marketing it or such other economic factors it believes are relevant in the circumstances. Patentees would be permitted to provide confidential commercial information in support of their position, including true prices in the PMPRB12 and proposed non-transparent rebates and discounts to direct and indirect payers in Canada. If the outcome of the above process is a determination that the price of the drug is potentially excessive:

- Its public ceiling price would continue to be set by international price referencing; but
- the ceiling price resulting from the application of the two-part test would be kept confidential.

Patentees will be required to report price and revenue information to the PMPRB net of direct or indirect third party discounts or rebates. This will ensure that the PMPRB is fully informed of the actual prices for patented drugs in Canada but also enable patentees to comply with much lower ceiling prices under the new framework.

## Part IV: Medium and low priority drugs

The fourth part of the new framework would apply to medium and low priority drugs. Drugs in this category would be expected to have a minimum number of therapeutic alternatives and offer little or no therapeutic improvement over the standard of care. Drugs considered to be medium priority would be subject to the same initial price test as high priority drugs, such that they would be considered potentially excessive if their public list price is above the median of public list prices in the PMPRB12 countries. For this class of drugs, the PMPRB could employ a revised therapeutic class comparison test that requires each successive entrant to reduce its price relative to the price of the drug that preceded it. Again, patentees would be provided with the opportunity to explain why a higher price is justified based on the same economic factors that are considered relevant for high priority drugs.

Drugs categorized as low priority, because of the presence of a significant number of therapeutic alternatives in the market and/or generic competition, would not be subject to an introductory or ongoing s.85 analysis and would be investigated on a complaints basis only.

## Part V: Re-benching

The fifth and final part of the new framework would involve the periodic "re-benching" of drugs to ensure that previous determinations of potential excessive pricing and/or price ceilings remain relevant in light of new indications (resulting in a change of market size) or changes in market conditions. Depending on the nature of the change, the re-benching process could result in a decrease or increase in ceiling price.

# CONCLUSION

If passed in their current form, the proposed amendments would allow the PMPRB to move to a risk-based framework that scrutinizes drugs with the greatest potential for excessive pricing and takes into account both their value to, and financial impact on, consumers in the health system when setting ceiling prices. This would constitute a paradigm shift in how the PMPRB regulates patented drug prices but would not depart from or expand on its original mandate.

By explicitly requiring the PMPRB to consider the new proposed factors, policy makers have recognized that price alone does not provide sufficient context by which to evaluate excessive pricing in the current climate. Specifically, price divorced from value, cost and affordability does not capture key inputs in determining what the impact of a drug will be on payers or on total population health. These are critical considerations in an era marked by increasingly constrained health budget envelopes, an aging population and an ever increasing number of drugs with annual average treatment costs in the hundreds of thousands of dollars.

It should be emphasized that the above described framework is only notional at this stage and may change as a result of any differences between the proposed amendments and the final Regulations or in response to stakeholder feedback from PMPRB-led consultations on Guideline reform.


# NEXT STEPS

In the coming weeks, Health Canada and the PMPRB will be hosting multi-stakeholder webinars where the department will address the proposed regulatory amendments and the PMPRB will address the changes discussed in this scoping paper. The PMPRB will also be making Guideline reform the focus of its upcoming annual outreach sessions for patentees to be held in January of 2018. It is expected that a first draft of the PMPRB's new Guidelines will be made public in the spring of 2018, with technical roundtables to be scheduled shortly thereafter. However, at this stage of the process, the PMPRB is specifically encouraging stakeholders to reflect on the following questions in order to prepare for upcoming consultations on a revised set of proposed Guidelines:

1. What considerations should PMPRB use in screening drugs for high priority?
2. To what extent should low priority drugs be scrutinized?
3. How should a cost effectiveness threshold be established?
4. Should the application of a threshold be subject to further adjustment depending on market size considerations?
5. How should re-benching work and when should it occur (and to what drugs)?
6. What price tests should the PMPRB apply to the new PMPRB12?
7. How should the PMPRB make use of confidential third party pricing information?

# FURTHER INFORMATION

Questions or clarifications on the content of this document can be submitted by email, letter mail or fax to:

**Patented Medicine Prices Review Board**
Box L40, 333 Laurier Avenue West, Suite 1400
Ottawa, Ontario  K1P 1C1
Fax: 613-952-7626
E-mail: PMPRB.Consultations.CEPMB@pmprb-cepmb.gc.ca

# Appendix 5.3: PMPRB Framework Modernization Presentation

Patented Medicine Prices Review Board | Conseil d'examen du prix des médicaments brevetés

# PMPRB Framework Modernization

***Presentation to Working Group***
***July 26, 2018***

Canada

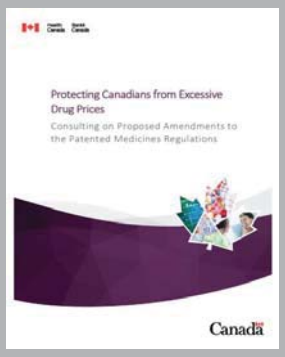
# Outline

- Summary of proposed regulatory amendments
- Overview of proposed New Guidelines framework
- Steering Committee Mandate

# We've been consulting since June 2016

**PMPRB Discussion paper on Guideline reform**


**Health Canada pre-consultation on regulatory amendments**




**Health Canada Gazette 1**


**PMPRB Guidelines scoping paper**




# The Current Regime

New patented drugs are assessed for level of therapeutic benefit relative to existing therapies and assigned a ceiling price that is based on either:

1. The median international price;
2. The highest price in the domestic therapeutic class, or;
3. Some combination of the two.

After entering the market, the price of a drug can increase in keeping with CPI but never to the point of becoming highest of the **PMPRB7**.

Where PMPRB staff and a patentee disagree about whether a new or existing drug is excessively priced, a hearing may be held before PMPRB Board Members.

If Members decide a drug is excessively priced, they can order the patentee to reduce its price and/or pay back excess revenues.

# Main problems with current framework

- Our basket of comparators – the **PMPRB7** - is made up of premium priced countries and includes the US, an international outlier.
- It is based on publicly available list prices, which are increasingly divorced from the true price net of confidential rebates/discounts.
- For many high cost drugs, the only factor the PMPRB can consider in setting the ceiling price is its public list price in the PMPRB7
- All drugs are subject to the same level of regulatory scrutiny, regardless of price/cost and market dynamics.
- Our only absolute ceiling for existing drugs is highest international price.



# Framework modernization

The three key changes being proposed will allow PMPRB to:

1. Compare prices to basket of countries that align more closely with Canadian context and priorities;
2. See what actual prices are being charged in Canada, so that whole regime isn't based on false values from the outset;
3. Consider the value of a drug and its potential impact on pharmaceutical spending in the price review process.

# Changing the basket of countries

Currently, the PMPRB checks the prices of patented drugs in 7 comparator countries to set the ceiling price of a new drug in Canada

The Government is proposing to include additional comparator countries and to drop the 2 outliers:

- United States whose drug prices are three times higher than other countries
- Switzerland whose GDP per capita is almost double that of Canada

| PMPRB-7 (existing basket) | |
|---|---|
| Country ([1]retained in new basket) | CDN Price Ratio |
| France[1] | 0.78 |
| Germany[1] | 1.00 |
| Italy[1] | 0.83 |
| Switzerland | 1.06 |
| Sweden[1] | 0.89 |
| United Kingdom[1] | 0.84 |
| United States | 2.91 |

| PMPRB-12 (new basket) | | | |
|---|---|---|---|
| Country ([2]added to new basket) | CDN Price Ratio | Country ([2]added to new basket) | CDN Price Ratio |
| Australia[2] | 0.78 | Norway[2] | 0.75 |
| Belgium[2] | 0.80 | South Korea[2] | 0.54 |
| France | 0.78 | Spain[2] | 0.80 |
| Germany | 1.00 | Sweden | 0.89 |
| Italy | 0.83 | United Kingdom | 0.84 |
| Japan[2] | 0.92 | | |
| Netherlands[2] | 0.79 | | |



# Regulating true prices

- When the PMPRB was created, actual prices paid in the market matched the public list prices
- Now, as a result of significant discounts and rebates to third-party payers, actual prices paid in the market are significantly lower than list prices
- Without access to this information, the PMPRB is unable to set ceiling prices that are actually meaningful to payers.

**Current**

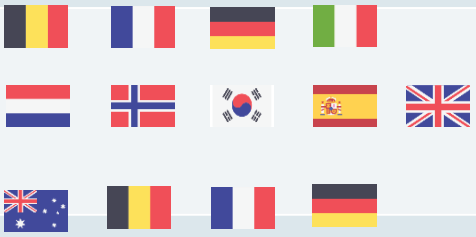
List Price - Rebates = Market Price

**Proposed**

List Price - Rebates = Market Price

# New pricing factors

Most other regulators look at additional factors beyond simply comparing prices paid in other countries, such as value for money and the size of the market

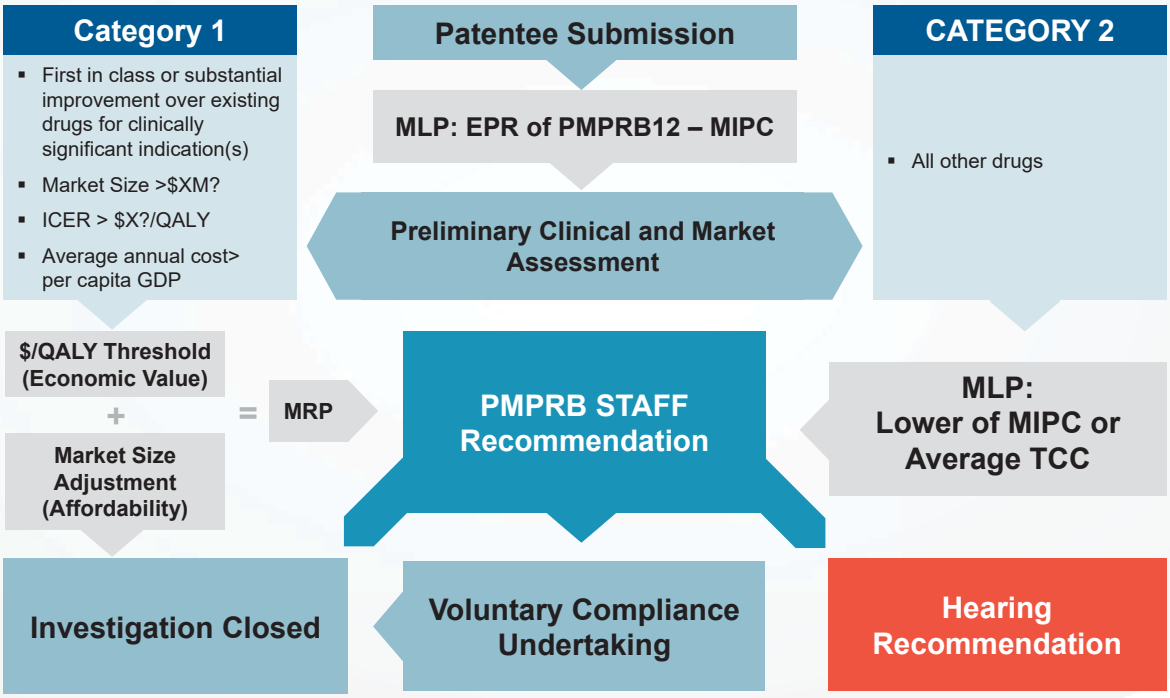
| Factor | Description | Comparator Countries Using the Factor |
|---|---|---|
| **Value for Money** | ▪ Comparison of the costs and benefits of a drug to patients and the healthcare system<br>▪ If paying for the drug would result in a net loss in total population health because it costs substantially more than existing drugs which provide the same or greater amount of health benefit, the price must come down |  |
| **Size of the market** | ▪ Consideration of ability-to-pay in Canada and the flexibility to re-assess subsequent changes in market size<br>▪ So, if a drug serves a significant number of patients, its high cost could make it unaffordable and limit access to a subset of the patient population |  |
| **Canadian GDP and GDP per capita** | ▪ Growth in GDP can be used as an indicator of the country's ability to pay while per capita GDP is a proxy for buying power at the level of the individual<br>▪ So, if the price exceeds the ability of Canada (measured by GDP) or Canadians (measured by GDP per capita) to pay for the drug, it may suggest that the drug price is excessive |  |



# Overview of new Guidelines framework

- A risk-based approach to price regulation that considers value and affordability, in addition to list prices in other like-minded countries.
- Basic structure can be broken down into 5 parts:
  - Part I: 'Maximum List Price' (MLP) for all new drugs at introduction based on median of PMPRB12 (MIPC)
  - Part II: Screening of drugs into high priority (Category 1) or low priority (Category 2)
  - Part III: 'Maximum Rebated Price' (MRP) for Category 1 drugs based on new pharmacoeconomic, market size and GDP factors
  - Part IV: Lower of MIPC and average of Therapeutic Class (ATCC) for Category 2 drugs
  - Part V: Re-benching
- The MLP will be a transparent ceiling based on public list prices but the MRP, which applies to Category 1 drugs only, will be confidential.
- To comply with the MRP, patentees of Category 1 drugs will be required to submit information on undisclosed rebates to third parties.

# Proposed PRICE Review Schematic






# Old vs new regime…

| Rule | How The Current Regime Works | How The Updated Regime Would Work |
|---|---|---|
| How international prices affect maximum prices in Canada | A new and improved drug cannot be priced higher than the median price of that same drug in the PMPRB7 | All new drugs cannot be priced higher than the median price of that same drug in the PMPRB12 |
| How domestic prices affect maximum prices in Canada | A new drug that isn't an improvement over existing drugs cannot be priced higher than the highest priced existing comparator drug in Canada | A new drug that isn't an improvement over existing drugs cannot be priced higher than the lower of the average price of existing comparator drugs in Canada and the median of the PMPRB12 |
| How inflation affects maximum prices in Canada | The price of a drug can increase every year with inflation. However, if a drug's price decreases in one year, its ceiling price the next year will be constrained by that decrease in price. | The ceiling price of a new drug is fixed at introduction. Prices can vary freely below this level in subsequent years. . |
| Changes to the maximum ceiling price after a new drug enters Canada | Once a new drug is given its ceiling price, it can only change through inflation or if the drug company voluntary lowers it. | The maximum price may be rebenched after a few years based on specific changes in market conditions. |

# Old vs new regime (continued)

| Rule | How The Current Regime Works | How The Updated Regime Would Work |
|---|---|---|
| **Pharmacoeconomics** | How much a drug costs for the amount of benefit it provides (e.g., $100 a pill for a year of healthy life) is not considered by the PMPRB in setting a maximum price | The cost-effectiveness of Category 1 drugs in terms of cost per quality-adjusted life year (QALY) is assessed against an evidence based threshold |
| **Market size and GDP*** | The total amount of money available to be spent on new drugs every year is not considered by the PMPRB in setting a maximum price | The market size of a new drug is a function of how much it costs and how many patients will need it. Drugs that are expected to have a significant market size and impact on the healthcare system will have a lower ceiling price to deter rationing. |

*Each year, the amount of money available to be spent on new drugs depends on total spending on drugs the year before and how much the economy is growing. For example, if Canada spent $1000 on drugs in 2018 and its economy grew by 2%, it would have $20 more to spend on the new drugs that come to market in 2019 (for a total of $1020)



# Part 1:Median international price test (MIPC)

- All new drugs are assigned a Maximum List Price (MLP) based on the median of the PMPRB 12 (MIPC).
- IMS will be used to verify international list prices.
- Category 1 drugs will be given both an MLP based on the MIPC and a Maximum Rebated Price (MRP)
- All other drugs will be deemed Category 2 and have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- No Category 2 drug will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).

# Part II: Screening

- Drugs will be screened into Category 1 if they are:

1. First in class or substantial improvement over existing therapy
2. Expected to have sales in excess of a $X million/year market size threshold
3. Above a $X/QALY threshold for clinically significant indications
4. Have an average annual treatment cost above per capita GDP.



# Part III: MRP for Category 1 drugs

- Step 1: application of pharmacoeconomic factor
  - Empirical work undertaken by Karl Claxton at the University of York suggests a $30K/QALY opportunity cost threshold for Canada.
  - Question whether and to what extent that estimate should be taken into account in at the screening phase to determine whether a drug should go in Category 1 or Category 2.
  - Category 1 drugs will then be subject to a baseline maximum value-based price ceiling of $X/QALY, for reasons of practicality and efficiency.
  - Drugs that meet certain clinical characteristics (e.g., high burden of disease or significant absolute gain in QALY) may be subject to a higher $/QALY ceiling.

# Part III: MRP for Category 1 drugs (continued)

- Step 2: application of market size and GDP factors
  - A Category 1 drug that meets the applicable $/QALY ceiling may still face an adjustment in price if the application of the market size and GDP factors raise affordability concerns.
  - Using new drug contribution to GDP and GDP growth over the last five years, the PMPRB is estimating a threshold of $XM per new drug.
  - New Category 1 drugs with an estimated market size that exceeds this threshold within any of its first five years of sale will require further price adjustments.
  - The adjustment would see the MRP reduced by a certain percentage discount which would increase as the expected market size increases (see next slide).
  - The market size threshold would also increase annually based on GDP growth and/or CPI.



# Application of new factors to Category 1 drugs – potential thresholds

| Type of review | $/QALY target to set MRP | Market impact adjustment |
|---|---|---|
| **Baseline New Drug (market size up to $20M)** | $60K | N/A |
| **"Premium" New Drug (e.g. high burden, EDRD, significant absolute QALY gain)** | $90K to $150K | N/A |
| **High Impact New Drug (market size over $20M)** | $60K | 10% reduction on MRP for each additional $10M market size (to 50% maximum) |

# Part IV: MLP for Category 2 drugs

- As mentioned, Category 2 and have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- However, no Category 2 drug will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).



# Part V: Re-benching

- All new drugs will be given an interim MLP of 3 years or until the drug is sold in 7 countries, whichever comes first.
- MLP is then frozen, as is MRP, unless re-benching is triggered by one of the following criteria:
  - Approval of a new indication
  - Sales in excess of expected market size
  - New evidence on cost-effectiveness (e.g. CADTH therapeutic class review or lifting of HC conditions on NOC)
  - Significant changes in international prices (eg. MIPC < MIPC at intro by more than 25%)
- Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI

# How compliance with new price ceilings will be assessed

- Price reviews will be conducted for the following customer classes:
  - National Retail – list price assessed against MLP
  - National Private Payer – average transaction price (ATP) assessed against MRP
  - Provincial Public Payer – ATP assessed against MRP in each market
- ATPs are calculated net of all discounts to determine compliance with confidential MRP.
- Category 2 drugs will be assessed against MLP.



# How pricing complaints will be managed

Complaints received by the PMPRB will trigger an investigation, during which the PMPRB will assess whether:

1. a drug is in compliance with the Guidelines; and
2. whether circumstances in the market have changed to warrant a rebenching/reclassification.

# Application of new Guidelines to existing drugs

- Existing drugs will be given an interim price ceiling based on the MIPC of the PMPRB12.
- An existing drug will only be classified as Category 1 if it fails a $X/QALY screen for any indication (would be higher than screen used for new drugs, for administrative and operational reasons).
- Existing drugs that are screened into Category 1 will be prioritized for re-benching.
- Category 2 drugs will be re-benched later unless a complaint is received.
- All drugs within a therapeutic class will be assessed at the same time for the purposes of the ATCC test.
- Patentees will be advised in advance of re-benching and given two reporting periods to come into compliance.



# PMPRB Guidelines Modernization Steering Committee

- The Steering Committee is being asked to provide targeted stakeholder feedback on key features of a new Guidelines framework which will serve the following dual objectives:

1. Operationalize amendments to the Patented Medicines Regulations designed to lower patented drug prices; and,
2. Support a risk-based approach to regulating drug prices that simplifies and streamlines compliance for patentees.

- In deliberating on the above, the Steering Committee should seek to strike a balance between the following guiding principles:
  - Sustainability
  - Predictability
  - Consistency
  - Functionality
  - Fairness
- The Steering Committee will be informed by the technical Working Group (the "**Working Group**").

# Suggested questions for Steering Committee

- Is the proposed division and treatment of Category 1 and Category 2 drugs a reasonable risk-based regulatory approach?
- Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?
- Should exceptions be made to the MLP-MIPC test and, if so, when and why?
- Should there be a price floor for Category 2 drugs based on LIPC?
- Should further drug categories exist with different treatment modalities from those proposed?
- Should more or less criteria be considered in screening a drug as higher risk and, where should the line be drawn with respect to the criteria?
- Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?
- Should Category 2 drugs be scrutinized more or less than proposed?
- Should the cost effectiveness threshold for Category 1 drugs vary?
- Should a Category 1 drug ever have more than one MRP?
- Are there economic considerations that would support a higher MRP for some Category 1 drugs than would result from the proposed application of the new factors?
- How often and in what circumstances should a drug be rebenched?
- Should confidential third party pricing information only be used for compliance purposes?
- Is there a better way to deal with existing drugs under the new framework?
- Are there opportunities to further reduce regulatory burden while respecting the dual objectives?

# Appendix 5.4: PMPRB Short Primer

# PATENTED MEDICINE PRICING REVIEW BOARD

*Prepared for the Working Groups on Guideline Reforms*

July 2018

The following short description is intended to address questions raised during the technical working group meeting about the PMPRB's mandate and role.

Prior to 1987, the Canadian Patent Act ("Act") allowed generic drug manufacturers to obtain compulsory licences to produce generic versions of patented brand name drugs at any time during the patent term. In addition, the Act only allowed for the patenting of processes to make medicines, but not the medicines themselves.

In 1987, the *Act* was substantially amended to reduce the availability of compulsory licences to generic manufacturers and to allow patents for the medicine themselves. These changes gave rise to a concern that patentees would abuse their newfound patent rights by charging prices above "reasonable" levels. To address this concern, the Act was further amended to create the PMPRB. All of these amendments were made to the Act through Bill C-22.

In introducing Bill C-22 in Parliament, the responsible Minister, the Hon. Harvie Andre, had the following to say regarding the dual intentions underlying the legislation:

> In essence, the amendments I propose in Bill C-22 will create a climate favourable to new investment in research and development in Canada by giving patent holding firms in Canada a guaranteed period of protection. These changes will also ensure consumer protection by creating a new prices review board to monitor drug prices…[1]
>
> There is the question of consumer protection. What good would come of it if we had all kinds of new drugs and no one could afford them? If the sick and elderly could not get access to the drugs, what good would come of it? …[2]
>
> I hereby submit that anybody who takes an objective view of what we are proposing will see that we have in place enormous checks and balances to ensure that consumer prices of drugs remain reasonable…[3]

Thus, while the purpose of stronger patent rights for pharmaceutical manufacturers is to incent innovation in Canada, the purpose of the PMPRB is to act as an effective check on these rights by

[1] House of Commons Debates, 33rd Parliament, 2nd Session, Vol. 1, page 1369, Hon. Harvie Andre (Minister of Consumer and Corporate Affairs).
[2] House of Commons Debates, 33rd Parliament, 2nd Session, Vol. 1, page 1371, Hon. Harvie Andre (Minister of Consumer and Corporate Affairs).
[3] House of Commons Debates, 33rd Parliament, 2nd Session, Vol. 1, page 1373, Hon. Harvie Andre (Minister of Consumer and Corporate Affairs).

ensuring that patentees do not charge excessive prices during the statutory monopoly period. The consumer protection the PMPRB provides extends to all Canadian purchasers of medicines, be they government, insurers, wholesalers or private individuals.

In a statutory monopoly situation, a seller has the ability to limit competition and thus can set a higher price than would otherwise exist, possibly to excessive levels. This risk of excessive pricing is exacerbated where demand for the product is high and there are few, if any, substitutes. In the pharmaceutical realm, this situation is most likely for patented medicines that are the first effective treatment of their kind for life threatening ailments. The PMPRB's existence as the only sector-specific regulator under the Act is attributable to this fact and a recognition by policy makers that the unfettered monopoly pricing of patented medicines is not in the public interest.

In 1993, the Act was amended again to eliminate the special compulsory licencing regime that had applied only to patented medicines and, as an offsetting measure, to provide the PMPRB with additional remedial powers in dealing with cases of excessively priced patented medicines. In speaking to the latter set of amendments, the sponsoring Minister, the Hon. Pierre Blais, explained to Parliament that their purpose was "to strengthen consumer protection, so that consumers can continue to obtain patented medicines at reasonable prices" and to "assure Canadian consumers, of reasonable prices, like those they have had since 1987."

The scope of the PMPRB's powers reside in sections 83 and 85 of the Act. Section 83 enables the Board to order a patentee to lower its maximum price where it is found to be "excessive".

> Where the Board finds that a patentee of an invention pertaining to a medicine is selling the medicine in any market in Canada at a price that, in the Board's opinion, is excessive, the Board may, by order, direct the patentee to cause the maximum price at which the patentee sells the medicine in that market to be reduced to such level as the Board considers not to be excessive

The Act does not define what an "excessive" price is, and instead directs the PMPRB to consider the following factors at section 85 in making that determination:

- the prices at which the medicine has been sold in the relevant market;
- the prices at which other medicines in the same therapeutic class have been sold in the relevant market;
- the prices at which the medicine and other medicines in the same therapeutic class have been sold in countries other than Canada;
- changes in the Consumer Price Index;
- *[proposed factor] the size of the market for the medicine in Canada and in countries other than Canada;*
- *[proposed factor] the gross domestic product in Canada and the gross domestic product per capita in Canada;*
- *[proposed factor] the pharmacoeconomic value in Canada of the medicine and that of other medicines in the same therapeutic class*

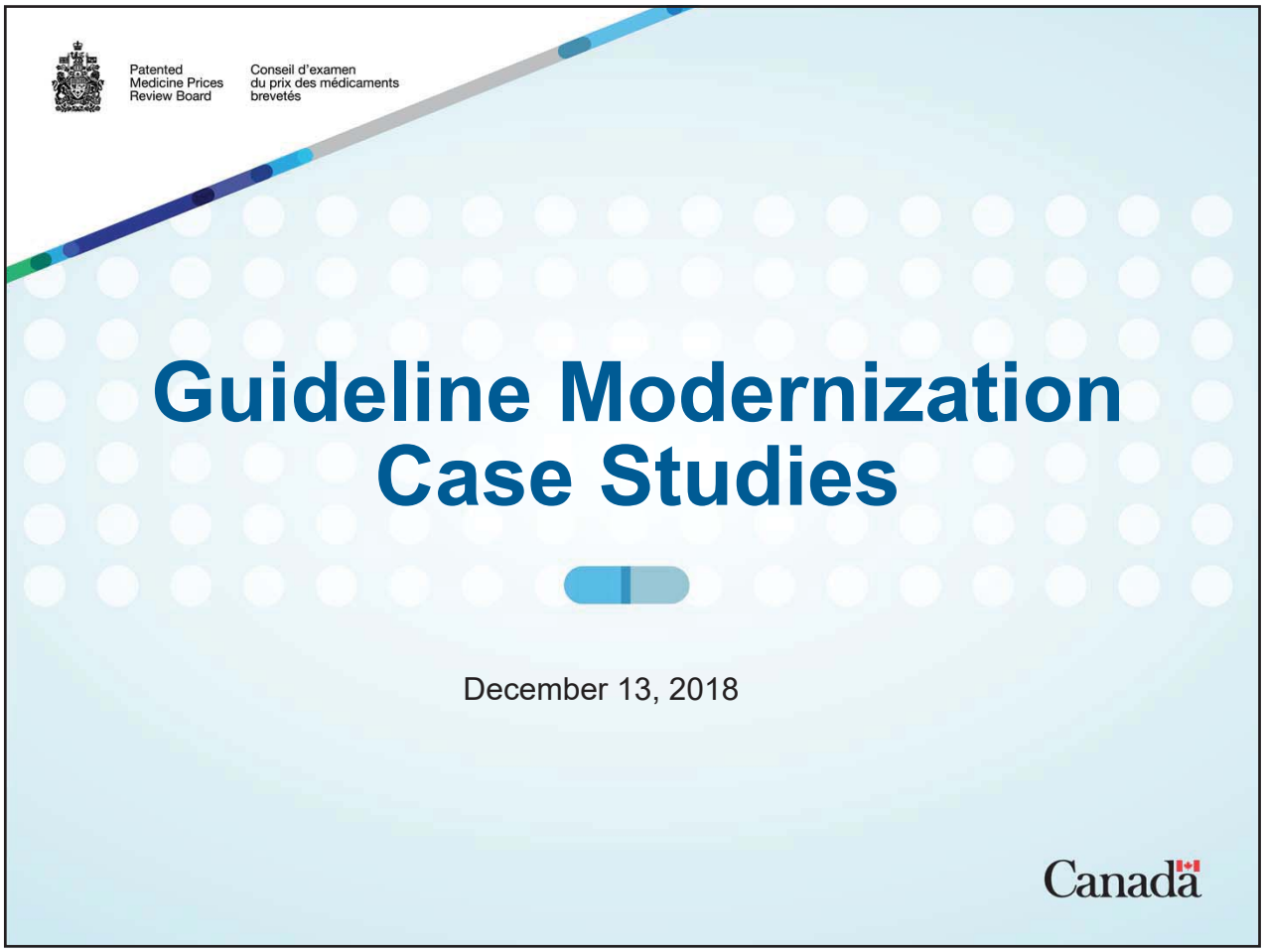
While the PMPRB can order price reductions following a hearing, it also issues Guidelines that outline how it monitors the prices of patented medicines to identify whether the price of any particular medicine should be considered potentially excessive and the subject of a hearing. The Guidelines are not binding, but they provide guidance on patentee pricing behaviour and adherence with the Guidelines reduces the likelihood that a patentee may find itself in a hearing before the Board.

Although it is part of the Health Portfolio, the PMPRB as a whole maintains an arm's length relationship with other entities including the Minister of Health and stakeholders. In other words, the PMPRB conducts its price monitoring and decides hearings independently from those entities. For example, while complaints from third parties may initiate an investigation under the Guidelines, the complainant has no part or role in the actual investigation or its resolution.

The PMPRB has no mandate or policy tools to incent innovation in Canada, cannot bar a patented medicine from being marketed in Canada; makes no decisions or recommendations regarding the approval of medicines for safety, efficacy and quality; and makes no decisions or recommendations regarding the listing or reimbursement of medicines in drug plans.

The Government believes that the PMPRB's current regulatory framework does not provide it with adequate tools to effectively protect Canadians from excessive prices, or for optimal identification of maximum prices in today's pharmaceutical environment. That is why Health Canada is advancing the proposed regulatory amendments, including new s.85 factors in the form of pharmacoeconomic value, market size and GDP.

# Appendix 6: Case Studies


Patented
Medicine Prices
Review Board
Conseil d'examen
du prix des médicaments
brevetés
Guideline Modernization
Case Studies
December 13, 2018
Canada

1

# Summary of Cases

| | Treatment cost (annual or full regimen) | Potential treatment population (annual) | Potential annual revenues | Profile | Potential disease area |
|---|---|---|---|---|---|
| Case 1 | $1K | 500,000 | $500M | Treats a chronic condition<br>One approved indication<br>Has comparators<br>Very large treatment population | Diabetes,<br>Mental health disorders |
| Case 2 | $7K | 100,000 | $700M | Treats a chronic condition<br>One approved indication<br>Substantial therapeutic benefit, no approved comparators<br>Large treatment population each year | AMD |
| Case 3 | $20K | 103,000 | $2B | Substantial therapeutic benefit to a less common chronic condition with a small treatment population<br>Moderate therapeutic benefit to a more common chronic condition with a large treatment population | DMARDs |
| Case 4 | $50K | 3,000 | $150M | One approved indication for 2nd line treatment of cancer<br>Several therapeutic alternatives exist<br>Small treatment population | Oncology |
| Case 5 | $50K | 200,000<br>(31,000) | $1.5B | Provides cure for a serious condition<br>Large treatment population<br>If no rationing, all could be treated in 7 years | Hep C |
| Case 6 | $300K | 1,000 | $300M | Rare disease drug with one indication<br>Limited clinical significance<br>Small treatment population, high severity of illness, unmet need | EDRD |

# Acronyms

HIPC – Highest international price comparison

MIPC –Median international price comparison

LIPC – Lowest international price comparison

TCC – Therapeutic class comparison

MLP – Maximum list price

MAPP – Maximum average potential price

MRP – Maximum rebated price

NEAP – Non-excessive average price

HTA – Health Technology Assessment

QALY – Quality-adjusted life year gained

ICER – Incremental cost-effectiveness ratio

PV – pharmacoeconomic value

$/QALY – cost per quality adjusted life years gained

RWE – Real world evidence



3

# Case 1 – Large population, therapeutic comparators

- Treats a chronic condition
- Has therapeutic comparators
- One approved indication by Health Canada (HC)
- Very large potential treatment population
  - Possible indications: diabetes, mental health disorders, etc.
- Annual treatment cost (list price): $1,000*
- Population with the condition: 500,000
- Potential annual revenues based on the total treatment population: $500M
- Category 1 due to market size

* Assumed a once-a-year dose for ease of calculations.



4

# Case 1 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $800 | $785 | $780 | $750 | $750 | $750 | $750 |
| PV Threshold Price** | N/A | $640 | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $33M | $50M | $68M | $75M | $81M | $91M |
| Market Size Adjustment *** | N/A | N/A | 10% | 30% | N/A | N/A | N/A |
| MRP | N/A | $640 | $627 | $581 | $581 | $581 | $581 |
| Total revenue at MRP | N/A | $33M | $49M | $61M | $68M | $74M | $82M |

*MLP/MRP frozen.
**CADTH estimated ICER is $100K. PV threshold used is $60,000/QALY.
***A progressive discount applies to the total annual drug cost (revenue) at the cost-effective price, where each successive $10M above $40M is discounted by an additional 10%, up to a maximum of 50%. This $40M market size threshold has been used for demonstration purposes only.

# Case 1 – Current vs New Proposed Guidelines

| Original ex-factory Price | $1,000 | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $1900 (assume top of TCC > MIPC) | Ex-factory price ceiling (MLP): $750<br><br>Rebated price ceiling (MRP): (frozen at year 3): $581 |
| Tests used to set the Ceiling | Midpoint of top of TCC and MIPC (moderate improvement) | MLP: MIPC<br>MRP: 30% adjustment to PV price |
| Ceiling percent reduction from original price | none | MLP: 25%<br>MRP: 42% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

## Case 2 – Large population, no therapeutic alternatives

- Treats a chronic condition
- One clinically significant approved indication
- No therapeutic alternatives
- Large treatment population
  - Potential disease areas: age-related macular degeneration (AMD).
- Annual treatment cost (list price): $7K
- Population with the condition: 100K in any given year
- Potential annual revenues based on the total treatment population: $700M
- Category 1 based on projected market size, no therapeutic alternatives



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# Case 2 –Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 |
|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $6.7K | $6.3K | $6.0K | $6.0K | $6.0K | $6.0K |
| PV Threshold Price** | N/A | $3,490 | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $67M | $97M | $125M | $80M | $97M |
| Market Size Adjustment | N/A | 30% | 50% | N/A | N/A | N/A |
| MRP | N/A | $3,050 | $2,525 | $2,525 | $2,525 | $2,525 |
| Total Revenue at MRP | N/A | $62M | $79M | $92M | $70M | $79M |

*MLP/MRP frozen at year 3.
**CADTH estimated ICER is $100K. PV threshold used is $60K/QALY.



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# Case 2 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$7,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $6000 | Ex-factory price ceiling (MLP): $6000<br><br>Rebated price ceiling (MRP): $2525 |
| Tests used to set the Ceiling | MIPC | MLP: MIPC<br>MRP: cost effectiveness adjusted for market size |
| Ceiling percent reduction from original price | 14% | MLP: 14%<br>MRP: 64% |
| Compliance assessment made against | ATP (rebated price, rebates include free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |



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## Case 3 – Two indications with different therapeutic benefits and prevalence rates

- Treats 2 chronic conditions
  - Condition 1 (first indication): estimated 3,000 people in Canada, first in class, brings significant therapeutic improvement over standard of care
  - Condition 2 (subsequent indication): Estimated 100,000 people in Canada, Therapeutic alternatives available, brings slight or no therapeutic improvement
- No therapeutic alternatives for condition 1, therapeutic alternatives for condition 2
- Annual treatment cost: $20K
- Potential annual revenues based on the total treatment population: $2B
- Category 1 based on projected market size.



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# Case 3 – Application of the Proposed Guidelines (first indication)

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $19K | $18K | $17K | $17K | $17K | $17K | $17K |
| PV Threshold Price *** | N/A | $9,975 | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $99M | $143M | $195M | $249M | $304M | $362M |
| Market Size Adjustment | N/A | 40% | 50% | 50% | N/A | N/A | N/A |
| MRP | N/A | $7,580 | $6,329 | $5,835 | $5,835 | $5,835 | $5,835 |
| Revenue at MRP | N/A | $80M | $102M | $128M | $163M | $199M | $237M |

*MLP frozen based on 7 countries.
**MRP frozen after 3 years.
*** ICER threshold used is $60K/QALY.



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# Case 3 – Application of the Proposed Guidelines (second indication)

Several therapeutic resulting in median TCC $6,000; LIPC = $14K

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MIPC | $19K | $18K | $17K | $17K | $17K | $17K | $17K |
| PV Threshold Price *** | N/A | N/A | N/A | N/A | N/A | N/A | N/A |
| MLP=higher of LIPC and median TCC | $14K | $13 | $12.5 | $12.5 | $12.5 | $12.5 | $12.5 |
| Revenue at MLP | $72M | $137M | $201M | $237M | $348M | $426M | $507M |
| Market Size Adjustment | N/A | 20% | 30% | 40% | N/A | N/A | N/A |
| MRP | $6,000 | $5,627 | $4,680 | $3,712 | $3,712 | $3,712 | $3,712 |
| Revenue at MRP | $31M | $59M | $75M | $81M | $103M | $126M | $151M |



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# Case 3 –Current vs New Proposed Guidelines

| Original ex-factory Price | $20,000 | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling Indication 1 | $19,000 | Ex-factory price ceiling (MLP): $17,000<br><br>Rebated price ceiling (MRP): $7,580 |
| Price Ceiling Indication 2 | $19,000 | Ex-factory price ceiling (MLP): $14,000<br><br>Rebated Price ceiling (MRP): $5,627 |
| Tests used to set the Ceiling | MIPC | MLP: MIPC for condition 1<br>LIPC for condition 2<br>MRP: lower of MLP or med TCC adjusted for market size for condition 2 |
| Ceiling percent reduction from original price | None | MLP: 10%; 26%<br>MRP: 60%; 70% |
| Compliance assessment made against | ATP (rebated price, rebates include free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |



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# Case 4 – 2nd line oncology medicine

- One clinically significant approved indication
- Several therapeutic alternatives exist
- Low 5-year survival rates
- Small treatment population: 3,000
- Annual treatment cost: $50,000
- Potential annual revenues based on the total treatment population: $150M
- Category 1 based on projected market size, annual treatment cost above GDP/capita



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# Case 4 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $47.5K | $45K | $42.5K | $40K | $40K | $40K | $40K |
| PV Threshold Price** | N/A | $25K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $10M | $15M | $19M | $25M | $30M | $36M |
| Market Size Adjustment*** | N/A | MIPC | MIPC | MIPC | MIPC | MIPC | MIPC |
| MRP | N/A | $45K | $42.5K | $40K | $40K | $40K | $40K |
| Revenue at MRP | N/A | $14M | $20M | $26M | $33M | $40M | $47M |

*MLP/MRP frozen.
**CADTH estimated ICER is $250K. PV threshold used is $60K/QALY.
***Positive market size adjustment owing to small market size – lower of MIPC, 2xPV Threshold price

# Case 4 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$50,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $45K (assume top of TCC < MIPC) | Ex-factory price ceiling (MLP): $40K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $40K |
| Tests used to set the Ceiling | Midpoint of top of TCC and MIPC (moderate improvement) | MLP: MIPC<br>MRP: Lower of MIPC, 2xPV threshold price |
| Ceiling percent reduction from original price | 10% | MLP: 20%<br>MRP: 20% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 5 – Curable condition, large treatment population

- Provides cure for a common and serious condition
- Large treatment population: estimated 200,000 Canadians are living with the condition
  - All could be treated in seven years assuming no rationing
- As of 2018, the health care system cost associated with the condition is estimated at $10 billion annually.
- Annual treatment cost of $50K (based on the manufacturer's suggested list price)
- Potential annual revenues based on the total treatment population: $1.5B
- Category 1 based on projected market size, annual treatment cost above GDP/capita



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# Case 5 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2* | End of Year 3** | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $48K | $45K | $43K | $43K | $43K | $43K | $43K |
| PV Threshold Price*** | N/A | $50K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $1.5B | $1.5B | $1.5B | $1.5B | $1.5B | $1.5B |
| Market Size Adjustment**** | N/A | 50% | 50% | 50% | 50% | 50% | 50% |
| MRP | N/A | $25K | $24K | $23K | $23K | $23K | $23K |
| Total revenue at MRP | N/A | $770M | $740M | $708M | $708M | $708M | $708M |

*MLP frozen based on 7 countries.
**MRP frozen.
***CADTH estimated ICER is $50K, below PMPRB PV threshold
****Maximum market size adjustment of 50%. Assuming competitor entry in Year 6.



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# Case 5 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$50,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $48K (assume top of TCC < MIPC) | Ex-factory price ceiling (MLP): $43K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $25K |
| Tests used to set the Ceiling | Higher of top of TCC and MIPC (substantial improvement) | MLP: MIPC<br>MRP: 50% adjustment to PV price |
| Ceiling percent reduction from original price | 4% | MLP: 14%<br>MRP: 50% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Case 6 – Rare disease drug

- Rare disease drug with one indication
- Limited clinical significance (moderate improvement over placebo) but offers hope for the first time for a severe condition with high burden of illness and high unmet need.
- Small treatment population: 1,000 Canadians diagnosed with the condition, 2% increase per year.
  - One in every 4,000 children born are affected by the condition.
- Annual treatment cost: $300,000
- Potential annual revenues based on the total treatment population: $300M
- Category 1 based on projected market size, annual treatment cost above GDP/capita



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# Case 6 – Application of the Proposed Guidelines

| Factor | Intro Period | End of Year 1 | End of Year 2 | End of Year 3* | End of Year 4 | End of Year 5 | End of Year 6 |
|---|---|---|---|---|---|---|---|
| MLP (set by MIPC) | $240K | $240K | $240K | $240K | $240K | $240K | $240K |
| PV Threshold Price** | N/A | $60K | N/A | N/A | N/A | N/A | N/A |
| Revenue at PV Price | N/A | $3.0M | $6.1M | $9.4M | $12.7M | $19.9M | $23.6M |
| Market Size Adjustment*** | N/A | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV | 2xPV |
| MRP | N/A | $120K | $120K | $120K | $120K | $120K | $120K |
| Total revenue at MRP | N/A | $6.0M | $12.2M | $18.7M | $25.4M | $39.8M | $47.2M |

*MLP/MRP frozen.
**CADTH estimated ICER is $300K-700K, depending on population and severity. Assume 80% price reduction required to meet PMPRB PV threshold of $60K/QALY.
***Positive market size adjustment owing to small market size – lower of MIPC, 2xPV Threshold price.



21

# Case 6 – Current vs New Proposed Guidelines

| **Original ex-factory Price** | **$300,000** | |
|---|---|---|
| | *Current Guidelines* | *Proposed Guidelines* |
| Price Ceiling | $240K | Ex-factory price ceiling (MLP): $240K<br><br>Rebated price ceiling (MRP): (frozen at year 3): $120 |
| Tests used to set the Ceiling | Midpoint of top of TCC and MIPC (moderate improvement, no comparators) | MLP: MIPC<br>MRP: 2xPV price |
| Ceiling percent reduction from original price | 20% | MLP: 20%<br>MRP: 60% |
| Compliance assessment made against | ATP (rebated price including free goods, but not PLAs) | MLP: ex-factory price<br>MRP: ATP where rebates include PLAs |

# Appendix 7: Disclaimers

## Appendix 7.1: Disclaimer from the PMPRB

The PMPRB provided the chair with the following disclaimer:

*"The views expressed herein are those of the author and of the parties to whom certain views are attributed and should not be understood to constitute or reflect the views of the PMPRB or the Government of Canada unless specifically stated."*

## Appendix 7.2: Disclaimer from Innovative Medicines Canada

Frédéric Lavoie provided the chair with the following disclaimer on behalf of Innovative Medicines Canada (IMC):

*"IMC understands that the PMPRB intends to take steps to modernize its Guidelines within the framework of the proposed amendments to the Regulations. While IMC is committed to constructive engagement with the PMPRB on Modernization of Price Review Process Guidelines, our participation on the Steering Committee and the Working Group should not be interpreted as supporting the proposed amendments to the Regulations. IMC continues to have serious policy and process concerns about the proposed amendments and reserves its right to oppose the proposed amendments and the work of the Steering Committee and Working Group to the extent it is intended to implement or reflect the proposed amendments. IMC also has many concerns with the June 25, 2018 Guideline Proposals and will provide more detailed commentary once we have had an opportunity to fully assess their potential impacts on patentees. With respect to the Working Group's governance, IMC intends to participate constructively but is concerned that minority and/or dissenting opinions should be fully and accurately placed on the record throughout the process including the draft and final report from the working group and the publication, following a request from one or more Working Group members."*

# Appendix 8: External Review of Draft Report

*The following is an external review of the draft report conducted by Dr Mark Sculpher from the Centre for Health Economics at the University of York.*

*This review was emailed to the chair on 4 March 2019.*

## General comments

Overall, the report reads well, and the guidance and advice offered to the PMPRB seems appropriate and well balanced.

> ***Chair's response**: I would like to thank Dr Sculpher for reviewing the draft report and providing a number of thoughtful comments. I have responded to each of these below.*

I have struggled to understand the role of PMPRB in relation to the CDR and provincial HTA arrangements. Presumably these different levels of policy review of drug prices will work synergistically and coherently. It seems to me that the most obvious version of such arrangements would be for PMPRB to set a ceiling price which CDR/provincial HTA to take as a maximum which may not be considered cost-effective from the perspective of a given province, indication or patient sub-group. In other words, PMPRB's ceiling price becomes a starting point for further evidence review, analysis and price negotiation that may very well bring prices down further. As such, some of the challenges considered in the report may well simplify (see below). Although this is not the remit of the report, there does seem to be a need to consider how PMPRB will work with CDR and provincial HTA, avoiding duplication and contradiction.

> ***Chair's response**: There are many possible approaches for setting a single ceiling price across multiple provinces, indications and/or patient subgroups. The Working Group recognized that the choice of which approach to adopt is a matter for policy makers. As a result, the Working Group did not advocate for any specific approach. Instead, we considered the technical implications of several possible approaches, in order to support policy makers in coming to an informed decision regarding which approach to adopt.*
>
> *Dr Sculpher proposes a specific arrangement under which the PMPRB first sets a ceiling price informed by the maximum price at which a medicine is 'just' cost-effective within a*

*single province, indication or patient subgroup, and then the price is negotiated down further using other mechanisms at the provincial level. The Working Group discussed some of the technical implications of such an arrangement. It was noted that provinces with lower supply-side thresholds might not have the negotiating power to bargain down the price to a level at which consumer surplus is positive for that province. As a result, such an approach might result in diminished population health in these provinces, which might in turn result in diminished population health across Canada as a whole.*

The report covers the key areas of evidence and analysis that I would have expected given the policy context, with three exceptions. The first is the importance of patient-level heterogeneity. There is considerable discussion about pricing by indication, but the same issues exist in relation to patient sub-groups within an indication. There is a trade-off between the product's ceiling price and the number of sub-groups for which it would be cost-effective. This is particularly obvious for products where cost-effectiveness is a function of the underlying risk of a clinical event (e.g. heart disease, osteoporosis etc), but it also applies to a large proportion of pharmaceuticals in other disease areas. I will come back to this below.

***Chair's response**: I agree with Dr Sculpher that patient heterogeneity within an indication is an important consideration. As a result of this heterogeneity, there might be specific patient subgroups within an indication that are more cost-effective to treat than others.*

*In principle, the implications for consumer and producer surplus of setting a single ceiling price across patient subgroups within an indication are similar to those associated with pricing across multiple indications (as considered in the Conceptual Framework). Among many possible approaches, the ceiling price might be informed by the price at which:*

1. *The most cost-effective patient subgroup is 'just' cost-effective to treat (resulting in negative overall consumer surplus within the indication in question);*
2. *The least cost-effective patient subgroup is 'just' cost-effective to treat (resulting in positive overall consumer surplus within the indication in question);*
3. *The 'average' patient within the subgroup is 'just' cost-effective to treat (resulting in zero overall consumer surplus within the indication in question).*

The second area where I would have expected more to be said relates to why there should be interest in producer surplus. A good deal of the report (most notably the first appendix on the conceptual framework) focuses on the balance between producer and consumer surplus, but the interest in the former is surely only because of its anticipated link with enhanced consumer

surplus in the future. The challenge is that there is little evidence on how much producer surplus is necessary to generate future consumer surplus, particularly in an individual and relatively small market. So much of what is in the report hinges on how much producer surplus (or probability of that surplus) should the system 'give away' now to incentivize research and development to generate future consumer surplus, but there is no discussion about how this might be determined given existing evidence.

> ***Chair's response**: It is for policy makers to decide upon the appropriate balance between consumer and producer surplus. The Working Group therefore did not take a position on whether greater producer surplus is inherently desirable or, as Dr Sculpher suggests, is desirable only if it results in greater consumer surplus in the future. Instead, the Working Group considered some of the potential implications for producer surplus associated with various possible approaches for informing a ceiling price.*

A related issue here is that the report often talks about consumer and producer surplus during a product's patent period as if it exists in perpetuity. For example, on page 26, in looking at the implications of a different supply-side thresholds across provinces. The implications of a patent ending for prices and consumer and producer surpluses under different policies seems relevant to consider.

> ***Chair's response**: The Working Group discussed the potential for prices to fall following patent expiry, with implications for the allocation of consumer and producer surplus over the long term. However, in a July 2018 document prepared for the Working Group (Appendix 5.4), the PMPRB clarified that the purpose of the PMPRB is to ensure that patentees "do not charge excessive prices during the statutory monopoly period". As a result, the Working Group focused only on the price during the statutory monopoly period.*

The final element of evidence and analysis on which I would have expected to see more relates to uncertainty. There is good coverage of the underlying challenges of uncertainty in the evidence and modelling and its implications for decision uncertainty, but I was surprised there was not more on policy responses to this and implications for ceiling prices. I am thinking here about frameworks that consider the value of additional evidence, whether evidence can be generated alongside reimbursement, the implications for irreversible costs and the importance of a product's price and its flexibility (e.g. Claxton *et al*). A reasonable response to this critique is that PMPRB only have one 'policy decision' in the domain of value and resources, namely setting a ceiling price. But more could perhaps have been said about what this means for

provincial HTA bodies which could, in principle, have other policy levers at their disposal such as funding only in research, funding alongside research and further price reductions.

***Chair's response**: I agree with Dr Sculpher that uncertainty has important implications for provincial decision makers, who may have a variety of policy levers at their disposal. However, the purpose of the Working Group was to provide specific technical recommendations to the Steering Committee regarding how the PMPRB might inform a ceiling price for a new medicine, so these implications were considered out of scope.*

## Specific comments

*Page 22:* The implication here is that supply side thresholds are only relevant to systems with a constrained budget. This is not the case: all systems have many other opportunities to enhance patient benefits, so incur opportunity costs when they make investment decisions (see Sculpher et al).

***Chair's response**: I agree with Dr Sculpher. The text on p.22 has been revised to remove reference to a "constrained budget".*

*Page 28:* It may be worth emphasising that any equity weights used as part of analysis supporting pricing and reimbursement decisions should also be applied to the empirical supply-side threshold.

***Chair's response**: I agree with Dr Sculpher that equity weights, if adopted, should also be applied to patients who bear the opportunity cost. Approaches for doing this include weighting the QALYs forgone directly, or adjusting the cost-effectiveness threshold. However, the latter approach has limitations that do not apply to direct QALY weighting.[19] The existing text notes that "there is also an ongoing and unresolved debate regarding whether weights should be applied directly to QALYs or to the cost-effectiveness threshold". I have not made any revisions to the text in response to this comment.*

*Page 29:* I was unclear how the PMPRB process would give information about the location of the demand curve if its focus is the maximum price a product should command in Canada. There would presumably also need to be information about the relationship between lower prices that might emerge from the provincial HTA process and volumes.

> ***Chair's response**: The Working Group recommended that "any estimate of the supply-side threshold adopted by the PMPRB for the purposes of informing a price ceiling be clearly specified, so as to reduce uncertainty for stakeholders" (Recommendation 2.7).*
>
> *This would provide information to stakeholders on the location of the demand curve, given the incremental cost and effectiveness of the medicine in question.*

Regarding the supply curve for new medicines, are there examples of any health system being able to estimate this credibly? I am not aware of any and, if that's the case, it would be helpful to reflect on its implications for the PMPRB process.

> ***Chair's response**: Difficulties associated with estimating supply curves, and some potential implications for the PMPRB, are noted throughout the Conceptual Framework. These implications include the potential that ceiling prices might be lowered to the extent that new medicines are not launched, potentially resulting in a loss in economic surplus and negating any positive consumer surplus that might otherwise have arisen.*

*Page 32*: There may be a case to mention in Section 2.3.9 the distinction between a policy threshold (i.e. the cost per QALYs (or its range) which generally leads to a positive funding/pricing decision) and an empirical estimate of the supply-side threshold. These are often confused in my experience and the examples of 'thresholds' quoted in this page are instances of the former rather than the latter.

> ***Chair's response**: I agree with Dr Sculpher. The text on p.32 has been revised to change all references to a non-supply-side "threshold" to "policy threshold".*

*Page 34-35*: This section could be repeated in the context of patient sub-groups by indication, but I saw no mention of this.

> ***Chair's response****: I agree with Dr Sculpher that individual level heterogeneity is an important consideration. However, since the Working Group did not explicitly consider approaches for setting a ceiling price across heterogeneous patient subgroups within a single indication, I have not modified the text in this section.*

I return to the point mentioned under 'general comments', that if PMPRB is defining a maximum price, then surely option 2 is appropriate. This would allow provinces to make decisions and undertake negotiations that involve bringing the price down so that other indications are also cost-effective.

This point could be generalised to cover deliberations regarding the choice of supply-side threshold (given variation across jurisdictions), patient sub-groups and reflecting uncertainty. That is, the PMPRB defines a maximum price, and the provinces may come down from that to reflect lower supply-side thresholds, agreement to include more sub-groups as well as indications, and the implications of uncertainty.

> ***Chair's response****: As noted earlier, the choice of which approach to adopt is ultimately a matter for policy makers. As a result, the Working Group did not advocate for any specific approach but instead explored the technical implications of several possible approaches.*

*Page 38*: I wonder whether invoking the concept of 'risk neutrality' and 'risk aversion' is helpful here. The underlying normative starting point for the report is a set of objectives relating to population health (perhaps augmented with equity considerations), rather than an unspecified utility function. What role is there, therefore, is considering risk preferences?

> ***Chair's response****: As noted in the Conceptual Framework, uncertainty raises the potential that the actual impact of a new medicine on population health at a given ceiling price is negative, even if the expected impact on population health is zero.*
>
> *If the PMPRB is 'risk neutral' then this is offset by the possibility that the actual impact on population health is positive, such that no adjustment is needed to the ceiling price.*

*However, if the PMPRB is adverse to the risk that the actual impact on population health is negative, then it may wish to lower the ceiling price. This would increase the expected impact on population health and reduce the risk that the actual impact is negative.*

*The latter position represents a departure from the default assumption of risk neutrality. However, the implied objective is still "related to population health (perhaps augmented with equity considerations)". Specifically, the implied objective is related not only to the expected population health but also the distribution of uncertainty around the expected population health, in both cases potentially augmented with equity considerations.*

*The Working Group was unaware of the PMPRB's precise risk attitude, and did not attempt to specify a "utility function" to account for any potential risk aversion. Rather, the Working Group acknowledged that the PMPRB might adopt an approach to risk that departs from the default assumption of risk neutrality, and noted that this would have implications for the specification of a ceiling price.*

*Page 45*: The term 'societal perspective' is used quite loosely here. It may be helpful to be more specific about what this means and how it aligns with a general normative starting point of objectives relating to population health and opportunity costs relating to health care resources.

***Chair's response**: On the previous page, reference is made to the CADTH guidelines which explicitly specify the differences between a 'public health care system' and 'societal' perspective (see "Differences between perspectives" on p.44).*

*I agree with Dr Sculpher that the use of a societal perspective raises important questions regarding the normative position with respect to population health and opportunity costs. As noted in the text, one Working Group member argued that "adopting a societal perspective implies that policy makers are willing to trade health benefits for other societal benefits, which may not be the case". Other members noted that a societal perspective raises "ethical concerns, including the potential for productivity to be valued less for those with lower earning power", which may not align with the preferred normative position. I have not made any modifications to the text in this section in response to this comment.*

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# Recommendations of the Working Group to Inform the PMPRB Steering Committee on Modernization of Price Review Process Guidelines


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# Overview

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- This presentation summarizes the recommendations of the Working Group to Inform the PMPRB Steering Committee on Modernization of Price Review Process Guidelines.
- Further details regarding the Working Group's activities, including its membership, process and procedure, a summary of deliberations, and 'on the record' comments from members, can be found in the Working Group's final report.
- This presentation was prepared by the chair of the Working Group following submission of the Working Group's final report to the PMPRB in March 2019.

# Terms of Reference

- The Terms of Reference (Appendix 4) required that the Working Group examine and make recommendations with respect to specific considerations and questions within the following six ‘areas of focus’:
    1. Criteria for classifying medicines as ‘Category 1’
    2. Supply-side cost effectiveness thresholds
    3. Multiple indications
    4. Accounting for uncertainty
    5. Perspective
    6. Market size factor

# 1. Criteria for classifying medicines as ‘Category 1’

# 1.1 Terms of Reference

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- *A Category 1 medicine is one for which a preliminary review of the available clinical, pharmacoeconomic, market impact, treatment cost and other relevant data would suggest is at elevated risk of excessive pricing. The following criteria have been identified as supporting a Category 1 classification:*
  - *The medicine is 'first in class' or a 'substantial' improvement over existing options;*
  - *The medicine's opportunity cost exceeds its expected health gain;*
  - *The medicine is expected to have a high market impact;*
  - *The medicine has a high average annual treatment cost.*
- *Should other criteria be considered? What are the relevant metrics for selecting medicines that meet the identified criteria and what options exist for using these metrics?*

# 1.3.1 No other criteria considered

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- No members of the Working Group proposed that any other criteria be considered beyond those specified in the Terms of Reference.

# Recommendation 1.1

Members voted
**12 in favour** and **0 against**

**The Working Group does not recommend any additional criteria beyond those specified in the Terms of Reference.**

# 1.3.2 ‘Substantial improvement over existing options’

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- A number of members expressed concern about the wording of Criterion A (*‘The medicine is ‘first in class’ or a ‘substantial’ improvement over existing options’*).
- Although there was general agreement that ‘first in class’ medicines should be classified as ‘Category 1’, many members questioned why medicines that offer *“a ‘substantial’ improvement over existing options”* should be classified as ‘Category 1’ if none of the other criteria are met.
- Concern was raised by some members that inclusion of this term might penalize manufacturers for producing medicines that offer ‘substantial improvement’, disincentivizing their development. Some members questioned whether this would, in turn, undermine the policy intent.

# 1.3.2 ‘Substantial improvement over existing options’

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- The chair asked the PMPRB to clarify the policy intent behind the inclusion of this term. The PMPRB responded that medicines that offer a ‘substantial’ improvement over existing options are more likely to dominate their respective market, increasing the risk of ‘excessive pricing’.
- Members of the Working Group were unable to identify examples of medicines which offer a ‘substantial’ improvement over existing options but would *not* be considered ‘first in class’ and would *not* have ‘high’ market impact or a ‘high’ average annual treatment cost. Even if inclusion of the ‘substantial improvement’ term is consistent with the policy objective, this raises the question as to whether its inclusion is redundant, given the presence of these other criteria.

# Recommendation 1.2

Members voted
**11 in favour** and **1 against**

**The Working Group recommends that the PMPRB consider whether the wording “substantial improvement over existing options” within Criterion A is redundant or inconsistent with the policy intent, and, if so, remove this from consideration.**

# 1.3.3 ‘Opportunity cost’ criterion

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- There was widespread agreement that Criterion B (*‘The medicine’s opportunity cost exceeds its expected health gain’*) should not be considered when classifying medicines as ‘Category 1’.
- Some members cited the logistical difficulty of establishing cost-utility estimates for all newly launched medicines, rather than only those classified as Category 1.
  However, since logistical issues were not within scope of the Terms of Reference, these issues were not considered by the Working Group.
- Another reason for excluding Criterion B, given by some members and consistent with the Conceptual Framework, is that this criterion may be redundant in the presence of the other criteria.

# Recommendation 1.3

Members voted
**11 in favour** and **1 against**

**The Working Group recommends that Criterion B be removed from consideration.**

# 1.3.4 ‘High average annual treatment cost’

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- There was disagreement amongst the Working Group regarding Criterion D (‘*The medicine has a high average annual treatment cost’*), specifically whether ‘high average annual treatment cost’ should be considered in absolute terms or as *incremental* upon existing treatment.
- It was noted that a new medicine could have ‘high average annual treatment cost’, but might replace an existing treatment that *also* has ‘high average annual treatment cost’, such that the *incremental* average annual treatment cost is not ‘high’.
- Some members noted that, if the *existing* treatment has ‘high average annual treatment cost’, this increases the risk that the existing treatment is itself considered to be ‘excessively priced’. In such cases, the new medicine may also be considered to be ‘excessively priced’, even if the *incremental* average annual treatment cost is not ‘high’.

# 1.3.4 ‘High average annual treatment cost’

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- As noted in the Conceptual Framework, the opportunity cost of adopting a new medicine is a function of its *incremental* cost compared to existing treatment.
- All else equal, the risk that adopting a new medicine will result in negative consumer surplus would therefore be expected to be greater for a medicine with high *incremental* average annual treatment cost, compared to a medicine with high *absolute* average annual treatment cost but low *incremental* average annual treatment cost.
- For this reason, the PMPRB may wish to consider ‘average annual treatment cost’ within Criterion D as being *incremental* upon existing treatment.

# 1.3.4 ‘High average annual treatment cost’

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- There are several considerations that would need to be be made when calculating this incremental cost:
  - The relevant treatment comparator would need to be established and the cost of treatment with the comparator estimated over the relevant time horizon.
  - If the comparator is itself a patented medicine, then consideration would also need to be given to any expected reduction in the cost of the comparator should generic alternatives to the comparator become available during the patent life of the new medicine.

# Recommendation 1.4

Members voted
**11 in favour** and **1 against**

**The Working Group recommends that “average annual treatment cost” within Criterion D be considered as incremental upon existing treatment.**

# 1.3.5 Relevant metrics

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- There was general agreement that the most appropriate metrics for each criterion would be those already used in Canadian practice.
- For example, if the PMPRB retains consideration of the ‘substantial improvement’ term in Criterion A, then the definition of ‘substantial improvement’ could be based upon the definition already adopted by the PMPRB.
- Other potential sources for definitions suggested by members included health technology assessment (HTA) and regulatory agencies in Canada.

# Recommendation 1.5

Members voted
**10 in favour** and **2 against**

**The Working Group recommends that the measures and definitions used for each criterion reflect existing Canadian practice.**

# 1.3.6 Determining a threshold for each criterion

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- There was some discussion regarding how to determine an appropriate ‘threshold’ to adopt for each criterion, building upon some potential thresholds proposed by the PMPRB.
- At the first meeting of the Working Group, the PMPRB proposed that, in considering Criterion B (‘*The medicine’s opportunity cost exceeds its expected health gain*’), the ICER could potentially be compared to a threshold of $30,000 per quality-adjusted life year (QALY).
- The PMPRB also proposed a potential ‘market impact’ threshold of either $20m or $40m, and proposed that a medicine could be considered to be of ‘high market impact’ if it reached this threshold in any one of either the first 3 years or 5 years after launch.

# 1.3.6 Determining a threshold for each criterion

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- Finally, the PMPRB proposed a potential ‘average annual treatment cost’ threshold of $50,000.
- The Working Group noted that the sensitivity of each criterion as a ‘screen’ is dependent upon the threshold adopted. The Working Group did not have the necessary data to calculate how many medicines would be classified as ‘Category 1’ under different combinations of thresholds across the criteria.
- Furthermore, it was noted that the ‘ideal’ number of medicines to classify as ‘high risk’ depends upon the PMPRB’s capacity for assessing ‘Category 1’ medicines (which was unknown to the Working Group), while the ‘ideal’ types of medicines to classify as ‘high risk’ depend upon the policy intent.

# Recommendation 1.6

Members voted
**10 in favour** and **2 against**

**The Working Group recommends that a threshold for each criterion be determined by the PMPRB, taking into account its capacity for assessing ‘Category 1’ medicines, the technical considerations of the Working Group, and the policy intent.**

# 1.3.7 Clear specification of the threshold for each criterion

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- The two industry members on the Working Group emphasized the importance of the PMPRB clearly specifying the threshold to be used for each criterion, so as to provide a “clear bright line” to manufacturers.
- A technical justification for this request is that a clear specification of the threshold for each criterion reduces uncertainty. The Conceptual Framework outlines how uncertainty in a medicine’s pharmacoeconomic value may result in an expected loss in economic surplus, such that there may be value in reducing this uncertainty. Similarly, uncertainty in whether a medicine may be subject to ‘Category 1’ classification may impose an expected loss on manufacturers and other stakeholders.

# Recommendation 1.7

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that the threshold for each criterion be clearly specified, so as to reduce uncertainty for stakeholders.**

# 2: Supply-side cost effectiveness thresholds

# 2.1 Terms of Reference

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- *Potential approaches for implementing a price ceiling based on a medicine's opportunity cost.*
- *Potential approaches for allowing price ceilings above opportunity cost for certain types of medicines (e.g. pediatric, rare, oncology, etc).*

# 2.3 Summary of Deliberations

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- The Working Group's deliberations on this topic were informed by two documents commissioned by the PMPRB prior to establishment of the Working Group:
  - A white paper prepared by the Institute of Health Economics (IHE) titled *"Theoretical models of the cost-effectiveness threshold, value assessment, and health care system sustainability*", hereafter referred to as the 'IHE report'.
  - A report prepared by Jessica Ochalek and colleagues from the University of York titled *"Assessing health opportunity costs for the Canadian health care systems"*, hereafter referred to as 'Ochalek *et al.* (2018)'.

# 2.3.1 Appropriateness of using a supply-side threshold

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- As noted in the IHE report, a supply-side threshold can be used to estimate the ‘health opportunity cost’ associated with adopting a new medicine within a public health care system. This health opportunity cost is measured in units of health benefit (typically QALYs) and reflects the estimated health ‘forgone’ by other patients within the health care system if limited resources are used to adopt the new medicine.
- For example, Ochalek *et al.* (2018) estimated a supply-side threshold of $30,000 per QALY for Canada as a whole, with some variation across provinces and territories. This estimate implies that every additional $30,000 spent on a new medicine results in one forgone QALY by other patients across Canada’s public health care systems.

# 2.3.1 Appropriateness of using a supply-side threshold

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- There was debate amongst Working Group members as to whether a supply-side threshold is always the most appropriate means for estimating the opportunity cost of new medicines. Specifically, consideration was given as to whether a ‘demand-side threshold’ might be more appropriate than a supply-side threshold in some cases.
- As noted in the IHE report, a demand-side threshold reflects Canadians’ ‘willingness-to-pay’ for health benefits. Some members argued that a demand-side threshold might therefore be a more appropriate threshold for private insurers and patients who pay out-of-pocket.
- Nevertheless, in light of the PMPRB’s clarification that the policy intent is to adopt the perspective of the Canadian public health care system, the focus of the Working Group’s deliberations was on a supply-side approach to estimating the threshold.

# 2.3.1 Appropriateness of using a supply-side threshold

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- Since the policy intent is to adopt the perspective of Canada's public health care systems, and since the Regulatory Impact Analysis Statement views the QALY, as used in cost-utility analysis, as the "gold standard" approach to considering the economic value of new medicines, it follows that the most relevant measure of the opportunity cost of a new medicine, given this policy intent, is an estimate of the QALYs forgone by patients within Canada's public health care systems.
- As noted in the Conceptual Framework, this may be estimated using an estimate of the incremental cost of the new medicine and an estimate of a supply-side cost-effective threshold, expressed in terms of cost per QALY.

# Recommendation 2.1

Members voted
**10 in favour** and **2 against**

**The Working Group regards the use of a supply-side cost-effectiveness threshold, as a means for estimating the opportunity cost of adopting new medicines within Canada's public health care systems, as consistent with the policy intent.**

# 2.3.2 Uncertainty in the empirical evidence base

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- The Working Group was unanimous in considering the empirical evidence base with respect to Canadian estimates of supply-side thresholds to be uncertain.
- The only existing estimate of a supply-side threshold for Canada is that provided by Ochalek *et al.* (2018). The authors acknowledged that this research was not primarily based upon Canadian data, noting that "*further research to provide Canadian and/or province specific elasticity estimates using within country and within province data should be regarded as a priority*".
- Some members of the Working Group expressed concerns with the instrumental variables (IVs) used by Ochalek *et al.* (2018).

# 2.3.2 Uncertainty in the empirical evidence base

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- One member noted that the authors employed two specific IVs that are potentially problematic:
  - Military expenditure per capita of neighbouring countries;
  - A measure of institutional quality, captured using:
    - The level of infrastructure (proxied by ‘paved roads per square km’);
    - Shock in ‘donor funding’ (absolute deviation from the historical mean).
- This member viewed the appropriateness of these IVs as questionable in the Canadian context.
- These potentially ‘weak’ IVs raise concerns about the parameter estimates from the authors’ regression model.

# Recommendation 2.2

Members voted
**12 in favour** and **0 against**

**The Working Group regards the current evidence base with respect to Canadian estimates of supply-side cost-effectiveness thresholds, including the empirical research by Ochalek et al. (2018), as uncertain.**

# 2.3.3 Direction and magnitude of bias in the $30,000 per QALY estimate

- Given the Working Group's concern with the IVs used in the Ochalek *et al.* (2018) research, members considered the potential direction and magnitude of bias in the $30,000 per QALY estimate.
- At a public seminar, the chair asked the corresponding author of the Ochalek *et al.* (2018) research, Dr Karl Claxton, for his views on the implications of any weakness in the IVs.
- Dr Claxton's response was that any weakness in the IVs would be expected to weaken the relationship between health expenditures and health outcomes, in turn resulting in an overestimate of the cost-effectiveness threshold.

# 2.3.3 Direction and magnitude of bias in the $30,000 per QALY estimate

- The implication of Dr Claxton's remarks is that a re-estimate of the supply-side threshold with stronger IVs would be expected to be below $30,000 per QALY.
- However, the Working Group member who initially questioned the strength of the IVs in the Ochalek *et al.* (2018) research disagreed, arguing that the direction of bias as a result of weak IVs is unknown.

# Recommendation 2.3

Members voted
**12 in favour** and **0 against**

**The Working Group regards the direction and magnitude of any bias in the $30,000 per QALY estimate by Ochalek et al. (2018) to be unknown.**

# Conceptual Framework

# Conceptual Framework

## A1.1 Foreword

This Conceptual Framework was drafted by the chair prior to the final meeting of the Working Group.

Its purpose was to guide the Working Group in making consistent recommendations across all six areas of focus, while respecting the policy intent and the range of views expressed by members of the Working Group throughout their deliberations.

# Conceptual Framework

## A1.1.1 Policy intent

During the Working Group's deliberations, the PMPRB stated that the most appropriate perspective to adopt when considering the 'pharmacoeconomic value' factor described in Amendment 4.4(a) in the Regulations Amending the Patented Medicines Regulations is that of *Canada's publicly funded health care systems*.

The Regulatory Impact Analysis Statement (Appendix 5.1) states that the *quality-adjusted life year (QALY)*, as used in cost-utility analysis, is regarded as the "gold standard" approach to considering the economic value of new medicines.

In a July 2018 document prepared for the Working Group (Appendix 5.4), the PMPRB clarified that the purpose of the PMPRB is to ensure that patentees do not charge excessive prices *during the statutory monopoly period*.

# Conceptual Framework

## A1.2 Economic principles

When considering how the price of any good ought to be determined, it is informative to consider some fundamental economic principles.

At any given price, the ‘economic surplus’ from a good is the sum of two parts:

- The ‘consumer surplus’, which is the benefit obtained by consumers because they are able to purchase the good at a price lower than their ‘willingness-to-pay’;
- The ‘producer surplus’, which is the benefit obtained by producers because they are able to sell the good at a price higher than their ‘willingness-to-accept’.

In order to consider the consumer and producer surplus that might arise from the PMPRB setting a ceiling price on a new medicine, we must first specify demand and supply curves.

# Conceptual Framework

## A1.2.2 Demand curve for a medicine

The demand curve reflects society's willingness-to-pay for the medicine in question.

The Working Group defers to the policy intent when considering the relevant components of the demand curve.

In light of the policy intent, a reasonable specification of the demand curve for a new medicine is based upon the net impact upon the lifetime health of patients associated with adopting the medicine within Canada's publicly funded health care systems for the duration of the statutory monopoly period, where health is measured in QALYs and discounted to a present value.

# Conceptual Framework

## A1.2.2 Demand curve for a medicine

The net impact of a new medicine upon patient health is a function of two components:

1. The gain in health experienced by patients who receive the new medicine; and
2. The loss in health experienced by other patients whose health care subsequently receives less funding than it would have done in the absence of the new medicine.

The gain in health for patients who receive the medicine is routinely calculated by CADTH and INESSS as part of their existing methods for conducting economic evaluations, and is typically denoted as ΔH (where the delta refers to ‘incremental’ and H refers to ‘health benefit’).

# Conceptual Framework

## A1.2.2 Demand curve for a medicine

The loss in health experienced by other patients is commonly referred to as the ‘opportunity cost’ of funding the new medicine.

The standard approach for estimating this health loss is to divide the incremental costs of the new medicine, commonly denoted as ΔC, by the ‘supply-side cost-effectiveness threshold’, typically denoted as *k*.

# Conceptual Framework

## A1.2.2 Demand curve for a medicine

Assuming that there is only one indication for the new medicine, and assuming a single value of *k* that applies regardless of the quantity of medicine supplied (assumptions reconsidered later), the demand curve for the new medicine is a perfectly elastic horizontal line that plots the ceiling price at which the health gain from the medicine is exactly offset by the health loss, such that the net health benefit is zero. That is, the demand curve plots the ceiling price at which:

$$\Delta H = \Delta C / k \qquad (1)$$

Rearranging equation (1), it follows that the demand curve plots the ceiling price at which the incremental cost-effectiveness ratio (ICER) of the new medicine is equal to *k*:

$$\Delta C / \Delta H = k \qquad (2)$$

# Conceptual Framework

## A1.2.2 Demand curve for a medicine

For the hypothetical medicine in Figure 1, the ICER is equal to *k* at a ceiling price of $P_1$, such that the demand curve is also plotted at this ceiling price.

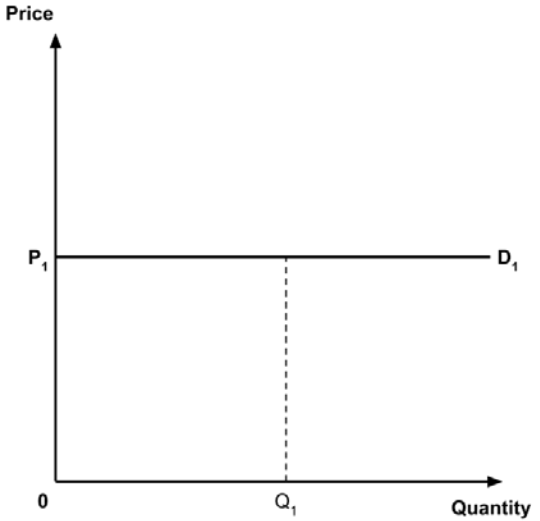


**Figure 1: Demand curve for a hypothetical medicine ($D_1$)**

# Conceptual Framework

## A1.2.3 Supply curve for a medicine

The supply curve plots the lowest price that a manufacturer would be willing to accept for a medicine.

This is sometimes referred to as the ‘reservation’ (or ‘reserve’) price of the medicine.

The supply curve is a function of a number of potential considerations, including the initial costs associated with developing the medicine, the marginal costs of production, and the potential implications for pricing in other jurisdictions as a result of ‘reference pricing’.

# Conceptual Framework

## A1.2.3 Supply curve for a medicine

Compared to the components of the demand curve (such as *k*), relatively little empirical research has been conducted into the components of the supply curve, with existing research focused primarily on estimating the costs associated with research and development (rather than the expected reservation price).

As a result of this asymmetry, the supply curve for each new medicine is highly uncertain.

For the purposes of this framework, the medicine's supply curve will therefore be treated as unknown (and plotted as a dashed line).

# Conceptual Framework

## A1.2.3 Supply curve for a medicine

Despite being unknown, we may reasonably expect the supply curve for a medicine to have the following basic properties:

1. A relatively high intercept on the vertical axis, reflecting the substantial initial costs associated with researching and developing the medicine;

2. A downwards slope, reflecting a declining per-patient cost of supplying the medicine as the quantity supplied increases. This declining per-patient cost arises from the ability to spread the initial costs of research and development across a greater number of patients, and also potential economies of scale in the production of the medicine.

# Conceptual Framework

A1.2.3 Supply curve for a medicine

Figure 3 plots possible supply curves for two hypothetical medicines.

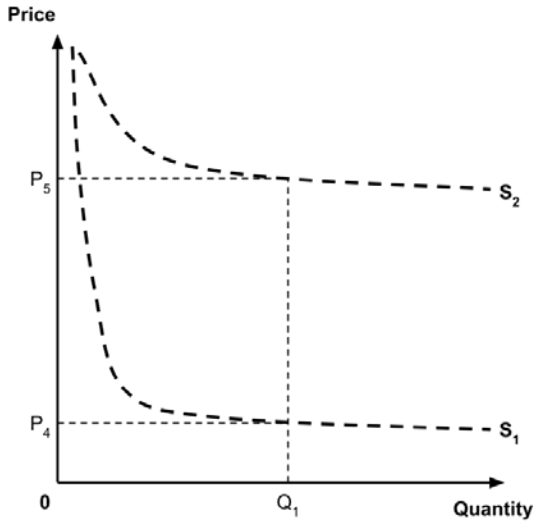


**Figure 3: Supply curves for two hypothetical medicines, with relatively low ($S_1$) and high ($S_2$) marginal costs of production**

# Conceptual Framework

## A1.2.4 Economic surplus

The demand and supply curves may be used to consider the ‘economic surplus’ that results from adoption of a new medicine and, at any given ceiling price, the distribution of this economic surplus between consumers (patients) and producers (the manufacturers of new medicines).

When demand and supply curves are plotted on the same figure, the economic surplus is illustrated by the area of the region below the demand curve and above the supply curve, minus any area above the demand curve but below the supply curve, and bounded between the vertical axis and the quantity of medicine adopted.

# Conceptual Framework

## A1.2.4 Economic surplus

For example, Figure 4A plots the demand ($D_1$) and supply ($S_1$) curves for a medicine with a relatively low supply curve. At a quantity of $Q_1$, the economic surplus is positive and illustrated by the area of region 2 minus the area of region 1.

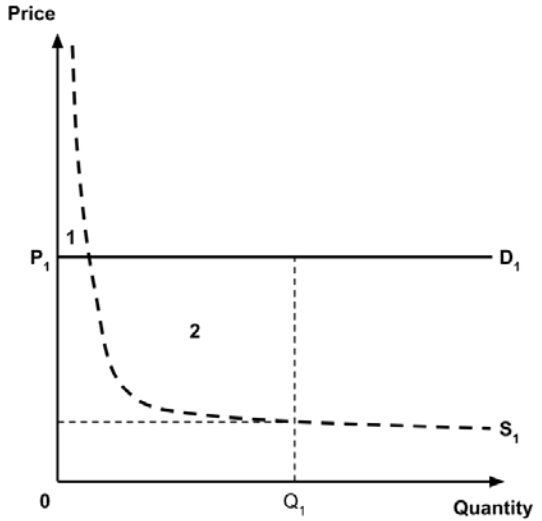


**Figure 4A: Demand and supply curves for a medicine with a relatively low supply curve, resulting in a positive total economic surplus**

# Conceptual Framework

## A1.2.5 Defining consumer and producer surplus

Given the policy intent, the ‘consumer surplus’ arising from adoption of a new medicine reflects the net health benefit (in QALYs) for patients within Canada’s public health care systems.

The ‘producer surplus’, meanwhile, reflects profits for the manufacturers of new medicines.

# Conceptual Framework

## A1.2.6 Allocating a positive economic surplus

If the economic surplus is positive then there is a range of possible ceiling prices at which consumer and producer surplus are both positive, such that adoption of the new medicine would provide a net benefit to patients and also the manufacturer.

# Conceptual Framework

## A1.2.6 Allocating a positive economic surplus

The upper bound of this range is a ceiling price corresponding to the demand curve ($P_1$), at which the ICER is *k*. At this ceiling price, the entirety of the economic surplus is allocated to the producer, such that the consumer surplus is zero.

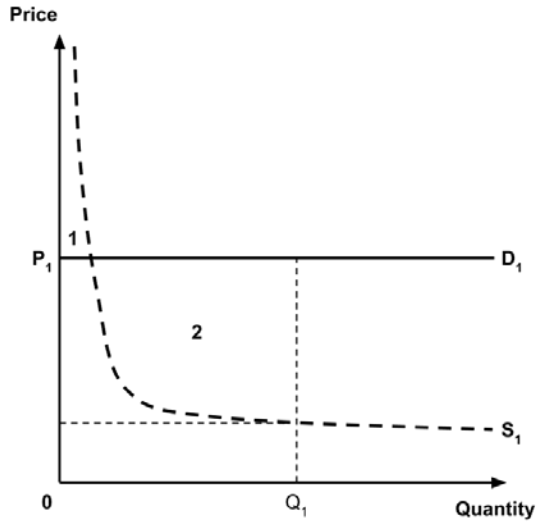


**Figure 5A: At a price of $P_1$, the entire economic surplus is allocated to the producer (region 2 minus region 1)**

# Conceptual Framework

A1.2.6 Allocating a positive economic surplus

The lower bound of this range is a ceiling price at which producer surplus is zero ($P_6$). At this ceiling price, the ICER is below k and consumer surplus is positive, illustrated by the combined area of regions 4 and 5. Producer surplus is zero.

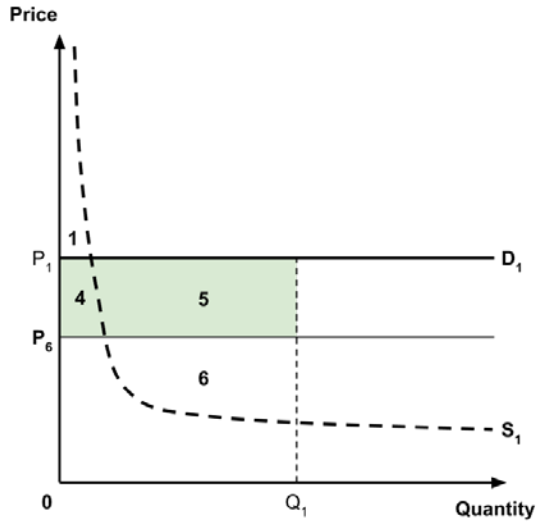


**Figure 5B: At a price of $P_6$, the entire economic surplus is allocated to the consumer (regions 4 and 5)**

# Conceptual Framework

## A1.2.6 Allocating a positive economic surplus

A ceiling price above $P_1$ (so the ICER exceeds *k*) would result in negative consumer surplus (such that the new medicine would diminish population health), and a ceiling price below $P_6$ would result in negative producer surplus (such that the new medicine is not profitable).

It follows that only a ceiling price between $P_1$ and $P_6$ in Figure 5B would result in both positive consumer surplus and positive producer surplus. At any ceiling price within this range, the ICER of the new medicine is lower than *k*.

Compared to the allocation of consumer and producer surplus which arises when the ceiling price corresponds to the demand curve (such that the ICER is exactly *k*), this allocation is closer to that which would arise in a conventional model of a competitive market.

# Conceptual Framework

## A1.2.7 Allocating a negative economic surplus

If the economic surplus is negative then there are no possible ceiling prices at which both consumer and producer surplus are positive. Although a higher ceiling price can be sought for the medicine at which producer surplus is positive, this will result in negative consumer surplus.

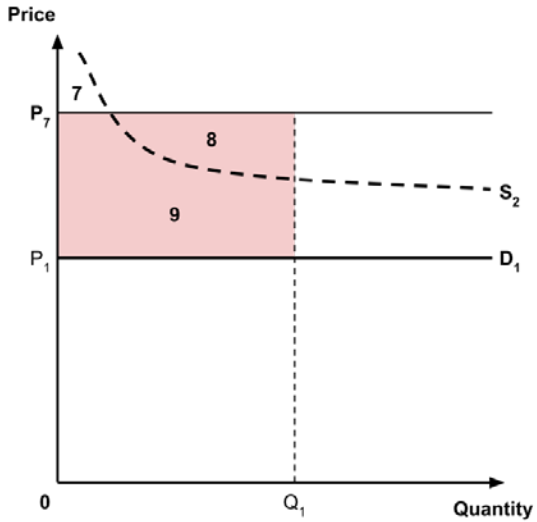


**Figure 6: Where the supply curve lies above the demand curve, producer surplus cannot be positive unless consumer surplus is negative**

# 2.3.4 Differences across provinces and territories

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- Several members noted that a different supply-side threshold would be expected for each Canadian public health care system.
- Theoretically, the supply-side threshold is affected by the budget of the health care system in question, among other considerations. Since each provincial and territorial health care system has its own budget, a different supply-side threshold would be expected for each.
- This is consistent with the results of the work by Ochalek *et al.* (2018), which found a different supply-side threshold (in terms of cost per DALY averted) in each province and territory.

# 2.3.4 Differences across provinces and territories

– – –

- The Working Group considered several potential approaches for setting a single ceiling price across all provinces and territories, including:
  - A ceiling price at which the medicine is ‘just’ cost-effective in the province or territory with the highest supply-side threshold;
  - A ceiling price at which the medicine is ‘just’ cost-effective in the province or territory with the lowest supply-side threshold;
  - A ceiling price at which the medicine is ‘just’ cost-effective across Canada as a whole.

# Conceptual Framework

## A1.3 Pricing across provinces and territories

Since the demand curve plots the ceiling price at which the ICER of the new medicine is equal to *k*, it follows that the demand curve will be higher in provinces and territories with larger estimates of *k*.

For example, based on the empirical work by Ochalek *et al.* (2018), we might expect the lowest demand curve in Prince Edward Island, the highest provincial demand curve in Alberta, and the highest demand curve overall in the Northwest Territories.

The width of each demand curve (the quantity demanded) would also be expected to differ across provinces and territories, since the number of patients receiving each new medicine will vary due to differences in population size and demographics.

# Conceptual Framework

## A1.3 Pricing across provinces and territories

Figures 7A to 7D demonstrate the implications of each approach considered by the Working Group using a simplified model of a new medicine provided to patients across two provinces.

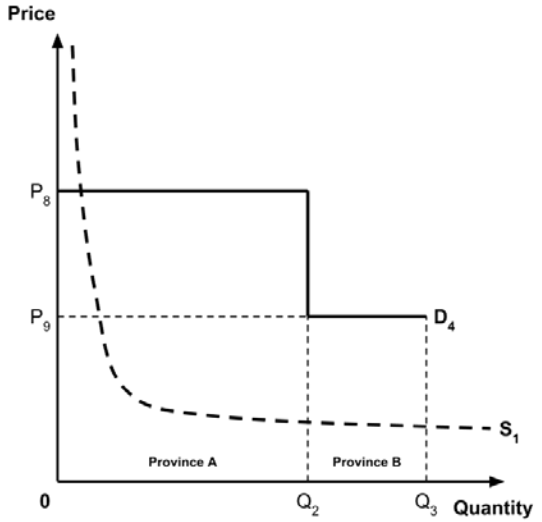


**Figure 7A: The demand curve for a medicine across two provinces**

# Conceptual Framework

A1.3 Pricing across provinces and territories

Approach 1: Set a ceiling price according to the highest *k*

Under the first approach, the ceiling price would be set at $P_8$ in both provinces (Figure 7B). This would result in no consumer surplus in ‘Province A’, but negative consumer surplus in ‘Province B’, such that the total consumer surplus is negative.

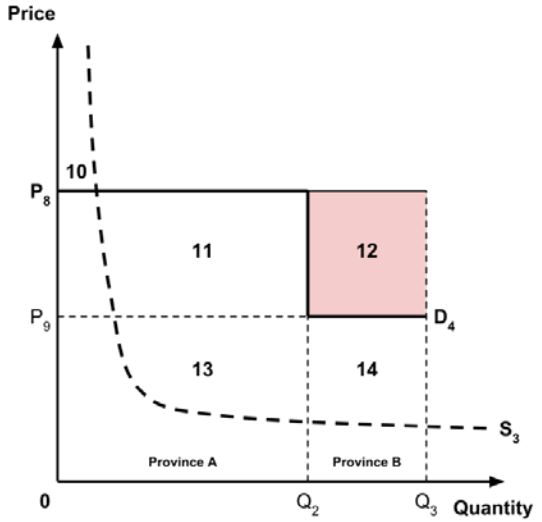


**Figure 7B: Under the first approach (ceiling price $P_8$), consumer surplus is negative in ‘Province B’ and zero in ‘Province A’, so negative overall**

# Conceptual Framework

A1.3 Pricing across provinces and territories

Approach 2: Set a ceiling price according to the lowest *k*

Under the second approach, the ceiling price would be set at $P_9$ in both provinces (Figure 7C). This would result in a positive consumer surplus in ‘Province A’, and no consumer surplus in ‘Province B’, such that the total consumer surplus is positive.

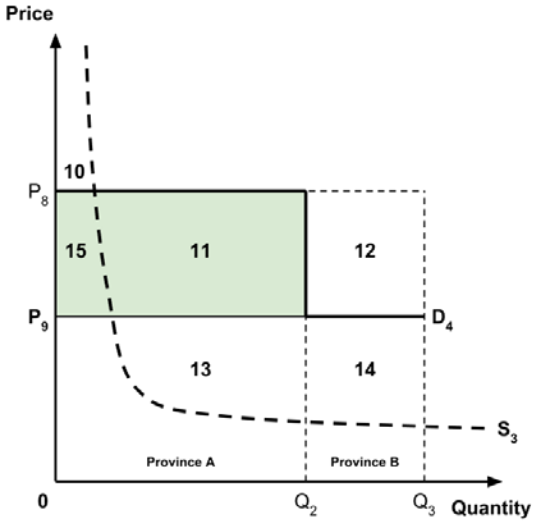


**Figure 7C: Under the second approach (ceiling price $P_9$), consumer surplus is positive in ‘Province A’ and zero in ‘Province B’, so positive overall**

# Conceptual Framework

A1.3 Pricing across provinces and territories

Approach 3: Set a ceiling price according to a weighted average of *k*

Under the third approach, the ceiling price would be set between $P_8$ and $P_9$ such that the total consumer surplus (across both provinces) is zero. In this example, this requires setting a ceiling price of $P_{10}$ (Figure 7D).

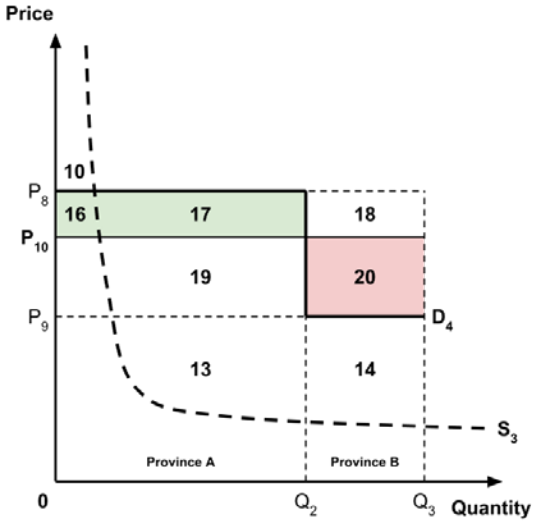


**Figure 7D: Under the third approach (ceiling price $P_{10}$), consumer surplus is positive in 'Province A'), negative in 'Province B', and zero overall**

# 2.3.4 Differences across provinces and territories

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- If the policy maker desires that new medicines *do not diminish population health across Canada as a whole*, such that overall consumer surplus is at least zero, then the first approach considered is inconsistent with this policy objective. The second approach comfortably satisfies this policy objective (since it results in positive overall consumer surplus), while the third approach only just satisfies this policy objective (since it results in an overall consumer surplus of zero).
- It follows that the ceiling price that arises under the third approach ($P_{10}$ in Figure 7D) is the maximum ceiling price that would be consistent with this policy objective.
- At this ceiling price, overall consumer surplus is zero, analogous to the consumer surplus arising in a standard model of a monopoly with perfect price discrimination.

# 2.3.4 Differences across provinces and territories

– – –

- If the policy maker instead desires that new medicines *do not diminish population health within any province or territory*, then both the first and third approaches are inconsistent with this policy objective. This is because both approaches result in diminished population health (negative consumer surplus) in at least one province or territory. The second approach would only just satisfy this policy objective, since consumer surplus is zero in the province or territory with the lowest *k*.
- It follows that the ceiling price that arises under the second approach ($P_9$ in Figure 7C) is the maximum ceiling price that would be consistent with this policy objective.

# 2.3.4 Differences across provinces and territories

– – –

- If the policy maker wishes to set ceiling prices for new medicines so as to *maximize population health across Canada as a whole*, then consideration should be given to the location of the supply curve:
  - If the supply curve is understood to be sufficiently high that the medicine would not be profitable at the ceiling price arising under the third approach, then it is not possible to specify a ceiling price at which the medicine is profitable and improves population health.
  - Alternatively, if the medicine is profitable at the ceiling price arising under the third approach, but is not profitable at the ceiling price arising under under the second approach, then maximizing population health requires specifying a ceiling price between $P_9$ and $P_{10}$.
  - Finally, if the supply curve is understood to be sufficiently low that the medicine would be profitable at the ceiling price arising under the second approach, then maximizing population health requires setting a ceiling price below $P_9$.

# 2.3.4 Differences across provinces and territories

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- Since the preferred allocation of the economic surplus is a matter for policy makers, the Working Group does not advocate for any specific approach.
- Instead, the Working Group recommends that any single threshold used for the purpose of informing a ceiling price be consistent with the policy intent, given the technical considerations outlined by the Working Group.

# Recommendation 2.4

Members voted
**12 in favour** and **0 against**

**The Working Group recognizes that each provincial and territorial public health care system has a unique supply-side cost-effectiveness threshold, and recommends that any single threshold used for the purpose of informing a ceiling price be consistent with the policy intent.**

# 2.3.5 Medicines with large net budget impact

- In theory, adopting medicines with a large net budget impact into a budget constrained public health care system would be expected to result in a disproportionately large opportunity cost. (Note that “net budget impact” is distinct from the “market size” consideration in section 6.)
- One approach for dealing with this is to use a progressively lower supply-side threshold for medicines with progressively larger net budget impact. One member cited the empirical work by James Lomas, which estimated how the supply-side threshold for the English NHS would fall as the net budget impact of a new health technology increases. For new hepatitis C treatments, Lomas found that the supply-side threshold would need to be adjusted down from £12,936 per QALY to £12,452 per QALY.

# 2.3.5 Medicines with large net budget impact

– – –

- The Working Group was unaware of any other attempts internationally to estimate supply-side thresholds associated with non-marginal changes in health expenditures.
- Since no equivalent empirical estimates are available for Canada, there is no data to inform such a downwards adjustment to the Canadian supply-side threshold at the present time.

# Recommendation 2.5

Members voted
**10 in favour** and **2 against**

**The Working Group recognizes that, in principle, a downwards adjustment should be applied to the supply-side cost-effectiveness threshold for medicines with substantial net budget impact, but notes that there is no Canadian empirical evidence to inform the magnitude of such an adjustment at the present time.**

# 2.3.6 Equity weights

- The Working Group noted that, under CADTH's 'reference case' requirements, all QALYs are assigned equal value. A justification of this position is provided in CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada' (4th Edition).
- CADTH's reference case therefore reflects an equity position under which a 'weight' of 1 is applied to all QALYs, regardless of any characteristics of the patients, disease or technology in question.
- Critically, a weight of 1 on all QALYs does not permit a ceiling price *"above opportunity cost"* for *"certain types of medicines"* but not others. The Working Group therefore considered the potential for applying different weights to some QALYs, and hence departing from CADTH's reference case assumption that all QALYs have equal value.

# 2.3.6 Equity weights

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- One member briefly summarized the small but growing empirical literature on the types of characteristics for which society may assign greater or lesser weight when valuing health gains.
- Characteristics that are often found to be important in empirical studies include severity of illness, the availability of active treatment alternatives, the prevalence of disease, the type of health gain (such as a reduction in pain), and the magnitude of health gain.
- These factors are often found to interact with one another, and so should not be considered independently.
- In the opinion of this member, greater empirical work is needed to fully understand these interactions and the ‘weights’ that would be put on each characteristic.

# 2.3.6 Equity weights

– – –

- Members also discussed theoretical issues associated with applying weights to some QALYs but not others.
- One member expressed concern that some important conceptual problems have not yet been addressed in the literature - for example, would a greater weight on QALYs for ‘cancer’ apply to all QALYs gained by a patient with cancer (including those gained through treatment for other diseases) or only the QALYs gained through cancer treatment (such that other QALY gains for the same patient for other diseases would be assigned different weight).
- There is also an ongoing and unresolved debate regarding whether weights should be applied directly to QALYs or to the cost-effectiveness threshold.

# 2.3.6 Equity weights

- As a result of these limitations in the empirical and theoretical literature, the predominant view of members was that equity weights other than 1 should not be implemented at the present time.
- There was some discussion by the Working Group regarding the potential implications of this recommendation for medicines for rare diseases.
- As noted in the Conceptual Framework, medicines with small market size may be expected to have a higher supply curve (at the respective quantity) than medicines with large market size.
- Such medicines may therefore be less profitable at a given ceiling price compared to medicines with larger market size. This issue is considered further in section 6.

# Recommendation 2.6

Members voted
**9 in favour** and **3 against**

**The Working Group does not recommend the implementation of 'equity weights' other than 1, as would be required to allow price ceilings above opportunity cost for some medicines but not others, due to limitations in the existing theoretical and empirical evidence base.**

# 2.3.7 Clear specification of the supply-side threshold

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- In common with the request that any thresholds used for classifying ‘Category 1’ medicines be clearly specified (section 1.3.7), the two industry members emphasized the desirability that any supply-side threshold used for the purposes of informing a price ceiling be clearly specified.
- As noted in the Conceptual Framework, the supply-side threshold is a key determinant of the location of the ‘demand curve’ for a new medicine. A technical justification for requesting that the supply-side threshold be clearly specified is that it reduces uncertainty for manufacturers regarding the location of this demand curve, and hence the producer surplus if the ceiling price is informed by this demand curve.

# 2.3.7 Clear specification of the supply-side threshold

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- There was general agreement among the Working Group about the desirability of specifying the supply-side threshold, and hence providing greater clarity to manufacturers and other stakeholders regarding the location of the demand curve.
- Nevertheless, as noted in the Conceptual Framework, there is also considerable uncertainty about the location of the manufacturer's 'supply curve'. This increases uncertainty regarding the set of possible ceiling prices at which consumer and producer surplus are both positive, potentially resulting in a loss of economic surplus for both consumers and producers. To minimize this uncertainty, efforts should be made to better understand the location of the supply curve for new medicines. This would complement efforts to provide greater certainty regarding the location of the demand curve through a clear specification of the supply-side threshold.

# Recommendation 2.7

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that any estimate of the supply-side threshold adopted by the PMPRB for the purposes of informing a price ceiling be clearly specified, so as to reduce uncertainty for stakeholders.**

# 2.3.8 Further empirical research

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- Given the uncertainties in the existing empirical evidence base regarding Canadian supply-side cost-effectiveness thresholds (sections 2.3.2 and 2.3.3), there was broad support among members of the Working Group for conducting further empirical research.
- Since differences in supply-side thresholds across provinces and territories are predicted by theoretical work and were observed by Ochalek *et al.* (2018) (section 2.3.4), there was also agreement that any future Canadian empirical studies should consider potential variation in estimates of supply-side cost-effectiveness thresholds across jurisdictions within Canada.

# Recommendation 2.8

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that the PMPRB support further empirical research to estimate a supply-side cost-effectiveness threshold for Canada. This research should consider and report on variation in estimates of supply-side cost-effectiveness thresholds across jurisdictions within Canada.**

# 2.3.9 Specifying an ‘interim’ threshold

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- Since the existing empirical evidence on Canadian supply-side thresholds was considered to be uncertain, and since further empirical research will take time to conduct and report, members discussed how a threshold might be specified by the PMPRB in the interim.
- One potential interim approach considered by the Working Group is for the PMPRB to specify a threshold in line with existing ‘policy thresholds’ used by Canadian HTA agencies. Taken together, the evidence considered by the Working Group suggests that informal policy thresholds used by HTA agencies in Canada are in the region of $50,000 to $100,000 per QALY, with oncology medicines assessed at the higher end of this range and other medicines assessed relatively lower within this range.

# 2.3.9 Specifying an ‘interim’ threshold

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- Another potential interim approach is to consider empirical estimates of supply-side thresholds for other jurisdictions with similar wealth and medicine market characteristics as Canada. The IHE report summarized three existing published estimates:
  - Claxton *et al.* (2015) estimated a threshold of £12,936 per QALY for the UK.
  - Vallejo-Torres *et al.* (2017) estimated a threshold of €21,000 to €25,000 per QALY for Spain.
  - Edney *et al.* (2017) estimated a supply-side threshold of AU$28,033 per QALY for Australia.
- The chair noted that the $30,000 per QALY estimate from Ochalek *et al.* (2018) is broadly in line with these estimates, and that all three of these countries are on the proposed PMPRB12 list of countries with *“reasonably comparable economic wealth”* and *“similar medicine market size characteristics”* as Canada.

# Recommendation 2.9

Members voted
**10 in favour** and **2 against**

**The Working Group recommends that any ‘interim’ threshold specified by the PMPRB prior to completion of further Canadian empirical work should be informed by a comprehensive consideration of existing thresholds used by Canadian HTA agencies and empirical estimates of supply-side thresholds from other relevant jurisdictions.**

# 3: Multiple indications

# 3.1 Terms of Reference

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- *Options for addressing medicines with multiple indications (e.g. multiple price ceilings or a single ceiling reflecting one particular indication).*

# 3.3 Summary of Deliberations

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- Two broad approaches were considered by the Working Group: a separate ceiling price for each indication (‘indication-specific pricing’), or a single ceiling price across all indications.
- There was general agreement that indication-specific pricing is the more appealing approach in principle. As noted in the Conceptual Framework, the incremental effectiveness of any medicine generally differs across indications. Indication-specific pricing would permit the ceiling price of the medicine to reflect this differing value for each indication. This would appear to closely align with the policy intent, as stated in the Regulatory Impact Analysis Statement, that “*the price paid for a medicine should take into consideration the value it produces”*.

# 3.3 Summary of Deliberations

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- However, although one member was of the view that multi-indication pricing may be feasible for some ‘Category 1’ medicines, several members expressed concern that indication-specific pricing is not possible in Canada, given current limitations in data capture and reporting.
- Since logistical and implementation issues were out of the scope of the Terms of Reference, Working Group members did not give detailed consideration to the feasibility of implementing indication-specific pricing in Canada.
- Instead, the Working Group’s deliberations focused exclusively on options for specifying a single ceiling price across multiple indications.

# 3.3.1 Specifying a single ceiling price across all indications

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- The Working Group considered several potential approaches for setting a single ceiling price across multiple indications, including:
  - A ceiling price at which the medicine is ‘just’ cost-effective in the most cost-effective indication;
  - A ceiling price at which the medicine is ‘just’ cost-effective in the least cost-effective indication;
  - A ceiling price at which the medicine is ‘just’ cost-effective across all indications;
  - A ceiling price at which the medicine is ‘just’ cost-effective in the first indication considered by the PMPRB.
- A consideration of the implications of each approach is provided in the Conceptual Framework.

# Conceptual Framework

## A1.4 Pricing across indications

Where a medicine is available for multiple indications, this has implications for specification of the demand curve for a new medicine.

If the per-patient health gain from the new medicine is different in each indication, then the ceiling price at which the ICER is equal to *k* will also differ across indications.

It follows that the demand curve will generally be different for each indication, with a relatively higher ceiling price corresponding to an ICER of *k* for those indications in which the medicine has a relatively greater per-patient health gain.

# Conceptual Framework

## A1.4 Pricing across indications

Figures 9A to 9D demonstrate the implications of each of these approaches using a simplified model of a new medicine provided to patients across two indications.

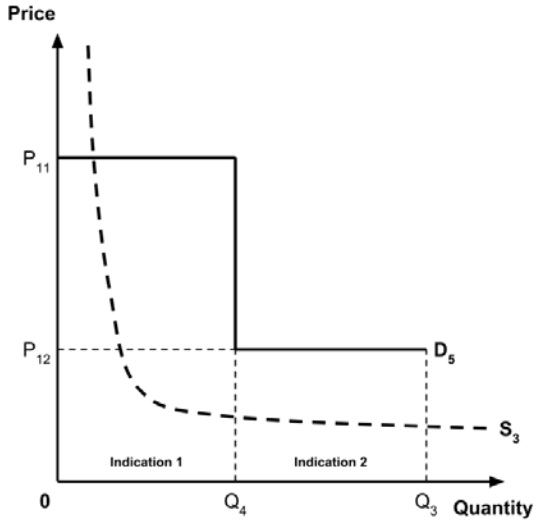


**Figure 9A: The demand curve for a medicine across two indications**

# Conceptual Framework

## A1.4 Pricing across indications

### Approach 1: Set a ceiling price based on the most cost-effective indication

Under the first approach, the ceiling price is set at $P_{11}$ across both indications (Figure 9B). This results in no consumer surplus in ‘Indication 1’, but negative consumer surplus in ‘Indication 2’, such that total consumer surplus is negative.

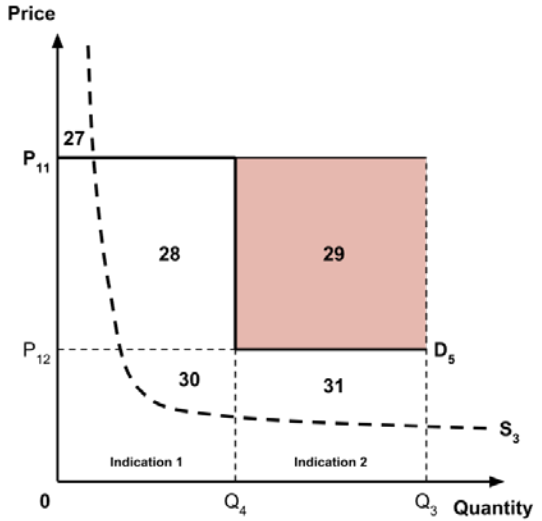


**Figure 9B: Under the first approach (ceiling price $P_{11}$), consumer surplus is negative in ‘Indication 2’ and zero in ‘Indication 1’, so negative overall**

# Conceptual Framework

A1.4 Pricing across indications

Approach 2: Set a ceiling price based on the least cost-effective indication

Under the second approach, the ceiling price is set at $P_{12}$ across both indications (Figure 9C). This results in positive consumer surplus in ‘Indication 1’, and no consumer surplus in ‘Indication 2’, such that total consumer surplus is positive.

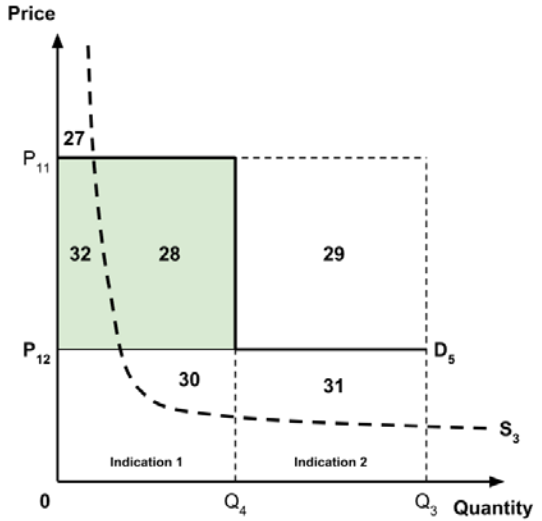


**Figure 9C: Under the second approach (ceiling price $P_{12}$), consumer surplus is positive in ‘Indication 1’ and zero in ‘Indication 2’, so positive overall**

# Conceptual Framework

A1.4 Pricing across indications

Approach 3: Set a ceiling price based on a ‘weighted average’ of all indications

Under the third approach, the ceiling price is set at $P_{13}$ across both indications (Figure 9D). This results in positive consumer surplus in ‘Indication 1’, but negative consumer surplus in ‘Indication 2’, such that total consumer surplus is zero.

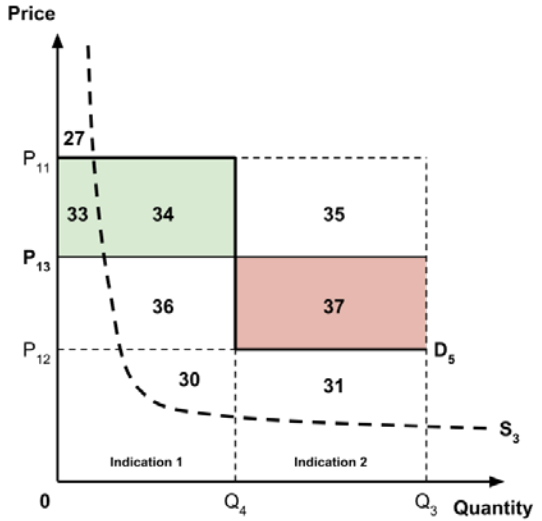


**Figure 9D: Under the third approach (ceiling price $P_{13}$), consumer surplus is positive in ‘Indication 1’, negative in ‘Indication 2’, and zero overall**

# Conceptual Framework

## A1.4 Pricing across indications

## Approach 4: Set a ceiling price based on the first indication considered

Under the fourth approach, the ceiling price would be set at either $P_{11}$ or $P_{12}$, depending upon which indication is first considered by the PMPRB.

Because producer surplus is unambiguously greater at a ceiling price of $P_{11}$ than $P_{12}$, this approach provides an incentive for the manufacturer to launch in the most cost-effective indication first (in this case ‘Indication 1’).

If manufacturers act upon this incentive, then this approach would have the same implications for consumer surplus as Approach 1.

If manufacturers do *not* act upon this incentive, this would have equivalent implications for consumer surplus as Approach 3.

# 3.3.1 Specifying a single ceiling price across all indications – – –

- If the policy maker desires that new medicines *do not diminish population health across Canada as a whole*, such that overall consumer surplus is at least zero, then the first approach considered is inconsistent with this policy objective. The second approach comfortably satisfies this policy objective, while the third approach only just satisfies this policy objective. The fourth approach *might* satisfy this policy objective if manufacturers are not strategic, but if manufacturers behave strategically then the expectation would be that consumer surplus is negative overall, in which case this approach would *not* satisfy this objective.
- It follows that the ceiling price that arises under the third approach ($P_{10}$ in Figure 7D) is the maximum ceiling price that would be consistent with this policy objective.

# 3.3.1 Specifying a single ceiling price across all indications

– – –

- If the policy maker instead desires that new medicines *do not diminish population health within any specific indication*, then both the first and third approaches are inconsistent with this policy objective. This is because both approaches result in diminished population health (negative consumer surplus) in at least one indication. Unless manufacturers consistently launch in the least-effective indication first, the fourth approach is also inconsistent with this objective. The second approach would only just satisfy this policy objective, since consumer surplus is zero in the province or territory with the lowest *k*.
- It follows that the ceiling price that arises under the second approach ($P_9$ in Figure 7C) is the maximum ceiling price that would be consistent with this policy objective.

# 3.3.1 Specifying a single ceiling price across all indications – – –

- If the policy maker wishes to set ceiling prices for new medicines so as to *maximize population health across Canada as a whole*, then (in common with the earlier consideration of this policy objective when pricing across provinces and territories) consideration should be given to the location of the supply curve.
- As before, the most desirable ceiling price under this policy objective is the lowest ceiling price at which producer surplus is non-zero. Depending upon the location of the supply curve, this might be at a ceiling price below $P_{12}$ in Figure 9D, leading to greater consumer surplus than that resulting from any of the four approaches considered above. However, as before, lowering the ceiling price to extract additional consumer surplus carries a risk that producer surplus may become negative, such that the medicine is not launched and consumer surplus is zero.

# 3.3.1 Specifying a single ceiling price across all indications

– – –

- At the final in-person meeting, the PMPRB asked the chair to consider a fifth potential approach for setting a single ceiling price across multiple indications:
  - A ceiling price at which the medicine is ‘just’ cost-effective in one specific ‘key’ indication identified by the PMPRB.
- The implications for the allocation of the total economic surplus depend upon whether the ‘key’ indication is more or less cost-effective than other indications:
  - If this ‘key’ indication is the most cost-effective, then the implications are the same as for the first approach, with negative overall consumer surplus.
  - Alternatively, if the ‘key’ indication is the least cost-effective, then the implications are the same as for the second approach, with positive overall consumer surplus.

# 3.3.1 Specifying a single ceiling price across all indications

– – –

- Since the preferred allocation of the economic surplus is a matter for policy makers, the Working Group does not advocate for any specific approach.
- Instead, the Working Group recommends that any single threshold used for the purpose of informing a ceiling price be consistent with the policy intent, given the technical considerations outlined by the Working Group.

# Recommendation 3.1

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that the PMPRB specify a single ceiling price for each medicine that applies across all indications and is consistent with the policy intent.**

# 4: Accounting for uncertainty

# 4.1 Terms of Reference

– – –

- *Options for using the CADTH and/or INESSS reference case analyses to set a ceiling price.*
- *Options for accounting for and/or addressing uncertainty in the point estimate for each value-based price ceiling.*

# 4.3.1 Using the CADTH and/or INESSS reference case analyses

- Members discussed how the results of pharmacoeconomic analyses of a medicine reported by CADTH, INESSS and other Canadian HTA agencies generally differ from those reported by the manufacturer and also from each other.
- The industry members argued that cost-utility estimates by CADTH and INESSS *“often exhibit differences in their estimates pertaining to heterogeneous assumptions and expert opinions”*, and that this variability is *“a function of the analyst that produces the assessment and the peer reviewers that challenge the analyses”*.
- Members also discussed whether the assumptions adopted by CADTH and INESSS in their ‘reference case’ analyses are appropriate for use by the PMPRB when setting ceiling prices.

# 4.3.1 Using the CADTH and/or INESSS reference case analyses

- Some members suggested that the PMPRB might wish to establish its own ‘reference case’, clearly specifying the requirements and any necessary assumptions for pharmacoeconomic analyses used to inform ceiling prices. Possible departures from existing CADTH and INESSS reference case assumptions include a clear specification of a supply-side cost-effectiveness threshold and a potential departure from the assumption of risk-neutrality (see section 4.3.3).
- Since matters of process were beyond the remit given by the Terms of Reference, the Working Group did not consider what specific processes might be established by the PMPRB to arrive at a single set of pharmacoeconomic results from which to inform a ceiling price. Nevertheless, there was a widespread view among Working Group members that clarity is required in whatever processes are established by the PMPRB.

# Recommendation 4.1

Members voted
**12 in favour** and **0 against**

**The Working Group recognizes that there is variation in the results of pharmacoeconomic analyses reported by CADTH and INESSS, and recommends that the PMPRB establish clear processes for identifying how these analyses will be used to inform a ceiling price.**

# 4.3.1 Ensuring unbiased estimates

- The Working Group noted that the most recent edition of CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada' (4th Edition) includes specific recommendations for addressing uncertainty in pharmacoeconomic analysis.
- These include an assessment of parameter uncertainty (through probabilistic analysis), structural uncertainty (through scenario analysis), and methodological uncertainty (through a comparison of 'reference case' and 'non-reference case' analyses).
- INESSS has similar requirements for considering uncertainty.
- Some members expressed concern that not all pharmacoeconomic analyses currently satisfy these recent CADTH guidelines, and that better enforcement of these guidelines is needed to ensure that uncertainty is appropriately addressed in all pharmacoeconomic analyses considered by the PMPRB when informing ceiling prices.

# 4.3.1 Ensuring unbiased estimates

- Members also noted that current HTA processes at CADTH and INESSS are undertaken for the purpose of assisting public payers in making decisions related to funding and informing pricing negotiations, rather than to inform ceiling prices set by the PMPRB. There was broad agreement that the PMPRB should engage with CADTH and INESSS, and any other relevant stakeholders, regarding modifications that may be required to these processes given the proposed change in the context of their use.
- While considerations of the specific processes adopted by CADTH and INESSS are beyond the scope of the Working Group, the key *technical* principle is that all pharmacoeconomic analyses should satisfy the same basic set of requirements, including a comprehensive and unbiased assessment of parameter uncertainty, structural uncertainty and methodological uncertainty.

# Recommendation 4.2

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that all pharmacoeconomic analyses used for the purpose of informing a ceiling price should satisfy the requirements of the most recent edition of CADTH's 'Guidelines for the Economic Evaluation of Health Technologies: Canada', including an unbiased assessment of parameter uncertainty, structural uncertainty and methodological uncertainty.**

# 4.3.2 Addressing uncertainty in the point estimate

– – –

- It was agreed that there are a number of sources of uncertainty in any pharmacoeconomic analysis. One member noted that clinical uncertainty is typically the primary source of uncertainty when CADTH considers new medicines, particularly for rare conditions. There are also uncertainties in the incremental costs associated with new medicines.
- Furthermore, since the supply-side threshold requires empirical estimation, it will inevitably be uncertain. For example, the UK research which estimated a supply-side threshold reported a probability distribution in addition to a point estimate.

# 4.3.2 Addressing uncertainty in the point estimate

– – –

- As noted in the Conceptual Framework, any uncertainty in the incremental costs and benefits results in uncertainty in the ICER. The price at which the ICER is equal to the supply-side threshold is also uncertain, resulting in uncertainty in the true location of the demand curve. This, in turn, results in uncertainty in the ceiling price that is consistent with the policy objective regarding the allocation of the economic surplus between consumers and producers.

# 4.3.2 Addressing uncertainty in the point estimate

– – –

- Members discussed how a ceiling price might be informed when there is uncertainty around the ICER. The standard approach for considering uncertainty in economic evaluations is to use the expected values of the incremental costs and incremental benefits in order to calculate an ICER. This is the approach adopted in CADTH's reference case, and implicitly assumes 'risk neutrality'.
- Members also debated using the upper bound of the credible interval around the ICER. Concern was raised that this approach would provide a disincentive for manufacturers to conduct research that reduces uncertainty around the ICER, since additional uncertainty would be rewarded with a higher ceiling price. It would also result in negative expected consumer surplus.

# Conceptual Framework

## A1.5 Uncertainty

This framework has so far assumed that ΔH, ΔC and *k* are known with certainty, such that a demand curve can be plotted at a fixed ceiling price within each province/territory and indication.

In practice, the estimates of ΔH and ΔC arising from probabilistic analyses conducted by CADTH and INESSS are uncertain, and hence the ICER of the new medicine is uncertain.

Furthermore, since *k* is subject to empirical estimation, this will also be uncertain.

# Conceptual Framework

## A1.5.1 Implications for the demand curve

Since both the ICER and k are uncertain, the ceiling price at which the ICER is equal to *k*, and hence the location of the demand curve, is also uncertain. Figure 11 reproduces the demand curve from Figure 1 with a 95% credible interval.

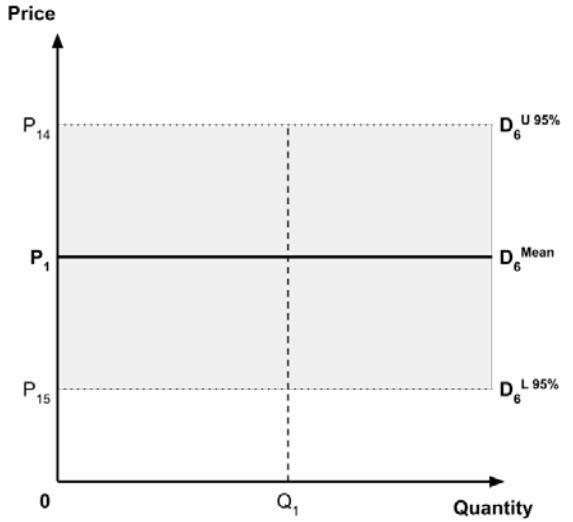


**Figure 11: Demand curve subject to a 95% credible interval**

# Conceptual Framework

## A1.5.2 Expected loss in economic surplus

If the *actual* ceiling price at which net health benefit (consumer surplus) is zero lies *above* the expected (mean) demand curve (as for $P_{16}$) then, provided the medicine is still launched, uncertainty results in *positive* consumer surplus (Figure 12A).

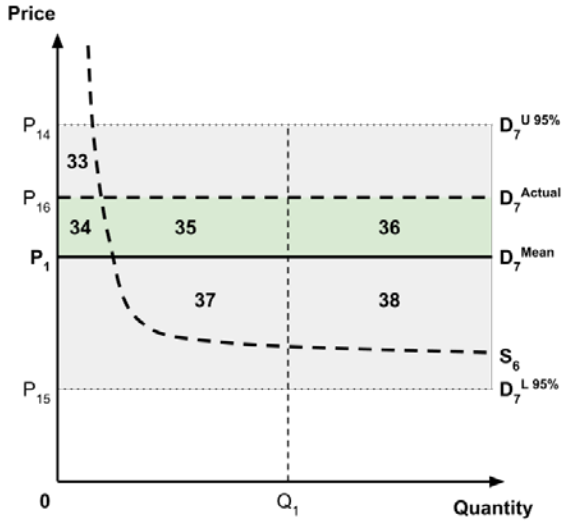


**Figure 12A: Example where the actual demand curve ($P_{16}$) lies above the expected demand curve ($P_1$) and the medicine is launched**

# Conceptual Framework

## A1.5.2 Expected loss in economic surplus

If the *actual* ceiling price at which net health benefit (consumer surplus) is zero lies *below* the expected (mean) demand curve (as for $P_{17}$) then, provided the medicine is still launched, uncertainty results in *negative* consumer surplus (Figure 12B).

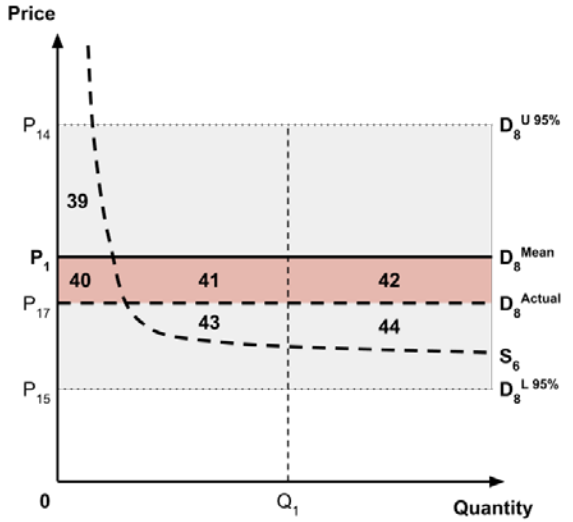


**Figure 12B: Example where the actual demand curve ($P_{17}$) lies below the expected demand curve ($P_1$) and the medicine is launched**

# Conceptual Framework

## A1.5.2 Expected loss in economic surplus

1. If the medicine is launched at a ceiling price coinciding with the *expected* demand curve then the *expected* consumer and producer surplus is zero.

2. If the medicine is unprofitable at a ceiling price coinciding with the *expected* demand curve, and is *also* unprofitable at a ceiling price coinciding with the *actual* demand curve, then the consumer surplus is zero.

3. If the medicine is unprofitable at a ceiling price coinciding with the *expected* demand curve, but would have been profitable at a ceiling price coinciding with the *actual* demand curve, then the impact of uncertainty is to *diminish* the total economic surplus such that *expected* consumer surplus at a ceiling price coinciding with the expected demand curve is *negative*.

It follows from this third result that uncertainty is associated with an expected loss in economic surplus.

# 4.3.2 Addressing uncertainty in the point estimate

– – –

- As noted in the Conceptual Framework, if the standard approach is adopted and a ceiling price is specified at which the ICER (calculated by dividing the expected incremental costs by the expected incremental QALYs) equals the expected value of the supply-side cost-effectiveness threshold, then the expected consumer surplus would be zero. (Note that the *actual* consumer surplus may be positive or negative, but the *expected* consumer surplus would be zero).
- If the policy intent is to ensure that expected consumer surplus is non-negative, and if a risk-neutral position is adopted, then this would be the highest ceiling price consistent with this policy objective.

# 4.3.2 Addressing uncertainty in the point estimate

– – –

- Alternatively, if a risk-adverse position is adopted, then a higher or lower ceiling price is required to mitigate this risk. Raising the ceiling price may reduce the risk that a medicine is not launched, while lowering the ceiling price may reduce the risk that a medicine results in negative consumer surplus.
- Since the PMPRB's risk attitude is not known, the Working Group cannot specify the most appropriate option for informing a ceiling price. Instead, the Working Group recommends that the PMPRB adopt an approach for considering uncertainty that is consistent with its risk attitude.

# Recommendation 4.3

Members voted
**10 in favour** and **2 against**

**The Working Group recommends that the PMPRB adopt an approach for considering uncertainty that is consistent with its risk attitude.**
**If the PMPRB is 'risk-neutral', this requires that the ceiling price be informed by the expected values of the incremental costs and QALYs for the medicine and the expected value of the supply-side cost-effectiveness threshold.**
**If the PMPRB is not 'risk-neutral', then consideration should be given to setting a ceiling price that is higher or lower than that under risk neutrality, given the policy intent.**

# 5: Perspectives

# 5.1 Terms of Reference

– – –

- *Options to account for the consideration of a public health care system vs societal perspective, including the option of applying a higher value-based price ceiling in cases where there is a ‘significant’ difference between price ceilings under each perspective.*
- *How to define a ‘significant’ difference in price ceilings between each perspective.*

# 5.3.1 Acknowledgement of policy intent

– – –

- Two months into the Working Group's deliberations, the PMPRB informed the Working Group that it had come to the view that a public health care system perspective *"needs to be used to meet the policy objective of the [Regulatory Impact Analysis Statement]"*.
- The PMPRB noted that, in coming to this view, it had benefited from the Working Group's discussions with respect to this area of focus.
- **Given this intervention from the PMPRB, the Working Group did not vote on any potential recommendations for this area of focus. Instead, the Working Group acknowledges that the policy intent is to adopt the perspective of Canada's public health care systems.**

# 6: Market size factor

# 6.1 Terms of Reference

– – –

- *Approaches to derive an appropriate affordability adjustment to a medicine's ceiling price based on an application of the market size and GDP factors (e.g. based on the US 'ICER' approach).*

# 6.3 Summary of Deliberations

– – –

- The Working Group noted that the *Proposed Regulatory Text* includes separate consideration of the pharmacoeconomic value, market size, and GDP factors.
- The ‘affordability adjustment’ that the Working Group was tasked with considering would therefore be applied separately from the consideration of ‘pharmacoeconomic value’.
- The proposed ‘affordability adjustment’ includes a potential upwards ceiling price adjustment for medicines with small market size and, independently, a potential downwards ceiling price adjustment for medicines with large market size.

# Conceptual Framework

## A1.6 Market size

We will now reconsider the demand and supply curves for a hypothetical new medicine from Figure 4A.

For simplicity, it is assumed that the medicine has a single indication and there are no differences in *k* across provinces and territories, such that there is a single horizontal demand curve ($D_1$) at a ceiling price of $P_1$.

It is also assumed that the ceiling price of the medicine is $P_1$, such that consumer surplus is zero (in the absence of a market size adjustment).

# Conceptual Framework

A1.6 Market size

Without any adjustments, $Q_6$ is the minimum market size at which the medicine is profitable. A smaller market size results in negative producer surplus, while a larger market size results in increasingly positive producer surplus.

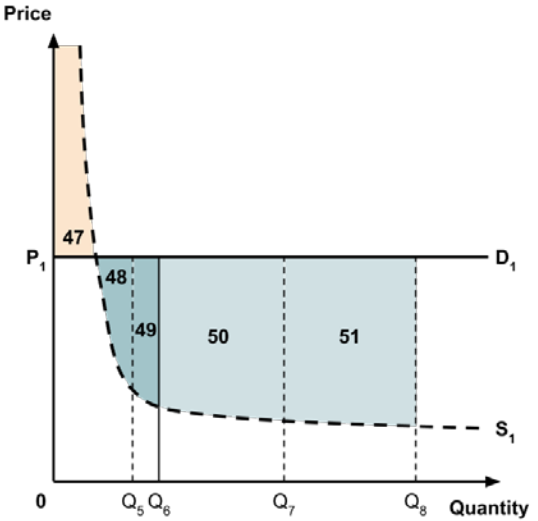


**Figure 13A: Without any 'market size adjustment'**

# Conceptual Framework

## A1.6.1 Implications of a market size adjustment

Following a hypothetical market size adjustment, medicines with market size below $Q_6$ receive a higher ceiling price, while medicines with market size above $Q_7$ receive a lower ceiling price.

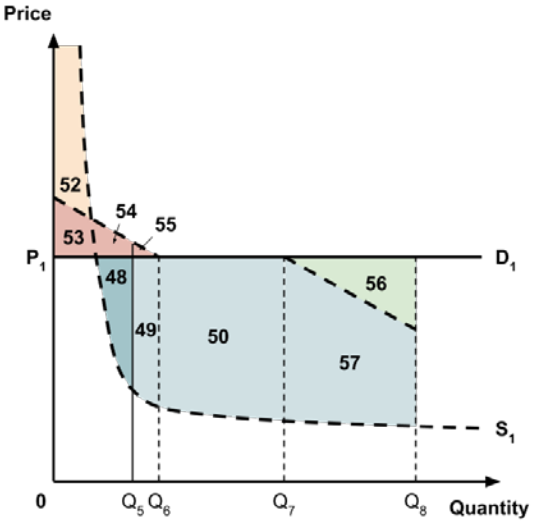


**Figure 13B: With a hypothetical 'market size adjustment'**

# Conceptual Framework

## A1.6.1 Implications of a market size adjustment

Implication 1: Increased consumer surplus from medicines with large market size

The reduction in the ceiling price for medicines with large market size results in an increase in consumer surplus (as illustrated by the area of region 56 for a medicine with market size $Q_8$).

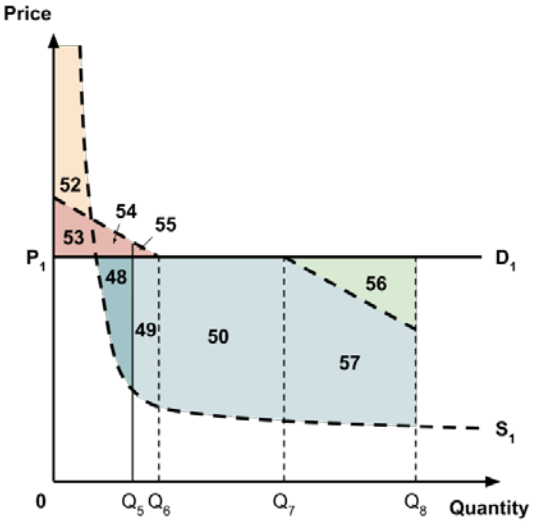


**Figure 13B: With a hypothetical 'market size adjustment'**

# Conceptual Framework

## A1.6.1 Implications of a market size adjustment

Implication 2: Reduced consumer surplus from medicines with small market size

A higher ceiling price for medicines with small market size results in greater producer surplus (as illustrated by the combined area of regions 53-55), but a correspondingly lower consumer surplus.

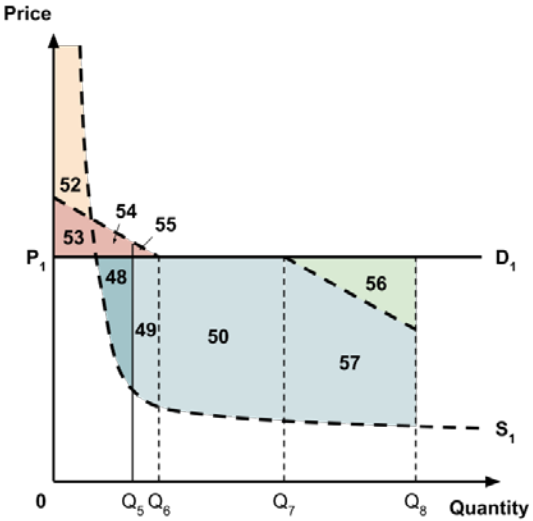


**Figure 13B: With a hypothetical 'market size adjustment'**

# Conceptual Framework

## A1.6.1 Implications of a market size adjustment

Implication 3: Increased profitability for medicines with small market size

The minimum market size at which a medicine is profitable has fallen from $Q_6$ to $Q_5$. This might, in turn, result in greater access to medicines with small market size.

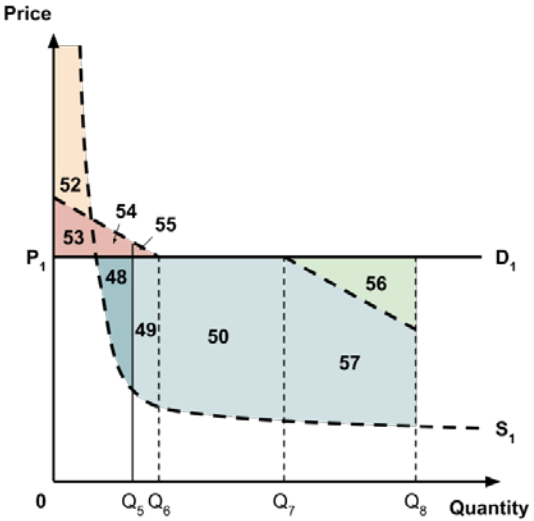


**Figure 13B: With a hypothetical 'market size adjustment'**

# 6.3.1 Implications for consumer and producer surplus

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- As shown in the Conceptual Framework, a downwards ceiling price adjustment for medicines with large market size would increase the consumer surplus, at the expense of producer surplus, associated with these medicines.
- An upwards ceiling price adjustment for medicines with small market size would increase producer surplus, at the expense of consumer surplus, for these medicines.
- Increasing the profitability of medicines with small market size might also result in greater access to such medicines. The potential for this is demonstrated in Figure 13B of the Conceptual Framework. This adjustment may therefore provide a means for mitigating the concerns expressed by one member regarding the potential impact of a lower ceiling price on access to orphan drugs (see section 2.3.7).

# 6.3.1 Implications for consumer and producer surplus

– – –

- Since the desired allocation of the economic surplus among consumers and producers is a matter for policy makers, the Working Group does not take a position on the appropriate magnitude of any proposed market size adjustments.
- Instead, the Working Group recommends that the PMPRB consider the implications of any proposed market size adjustments for the allocation of the economic surplus, and ensure that these are consistent with the policy intent.

# Recommendation 6.1

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that the PMPRB consider the implications of any market size adjustments for the allocation of consumer and producer surplus, and ensure that these are consistent with the policy intent.**

# 6.3.2 Potential incentives and disincentives

- The Working Group discussed several potential incentives and disincentives associated with implementation of a market size adjustment.
- It was noted that the estimated market size of a medicine at launch is uncertain. A market size adjustment based on a medicine's estimated market size might therefore result in a downwards adjustment to the ceiling price for a medicine which does not ultimately achieve a large market size. Conversely, a downwards adjustment might not be applied to a medicine that unexpectedly achieves a large market size. To minimize any resulting disincentives, the market size adjustment would ideally be applied to actual market size rather than expected market size.

# 6.3.2 Potential incentives and disincentives

– – –

- If the reduction in ceiling price for medicines with large market size is large, then manufacturers may be incentivized to reduce the quantity supplied so as to avoid the reduction in the ceiling price.
- By providing a higher ceiling price for medicines with low market size, a market size adjustment might also relatively incentivize the development of such medicines. Over time, a reduction in medicines with large market size and an increase in medicines with small market size might result in progressively smaller gains and progressively larger losses in consumer surplus.

# Recommendation 6.2

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that the PMPRB consider the potential incentives and disincentives that might result from the application of any market size adjustments.**

# 6.3.3 GDP and GDP per capita

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- The Working Group discussed how any thresholds specified for the criteria used to classify medicines as ‘Category 1’, as well as any supply-side threshold specified by the PMPRB, may need to be periodically revised in response to changes in GDP and GDP per capita over time.
- A change in GDP or GDP per capita over time would be expected to have an indirect impact upon the supply-side threshold through a change in the size of the health care budget. It follows that the supply-side threshold should not be adjusted directly to account for changes in GDP or GDP per capita; rather, it should be recalculated periodically to reflect changes in the size of provincial and territorial health care budgets and the marginal productivity of health care services that face displacement from the adoption of new medicines.

# Recommendation 6.3

Members voted
**12 in favour** and **0 against**

**The Working Group recommends that the PMPRB periodically reconsider any specified thresholds in response to changes in GDP and GDP per capita over time, including the supply-side cost-effectiveness threshold and any thresholds for criteria used to classify medicines as ‘Category 1’.**

# 6.3.4 Considerations beyond ‘pharmacoeconomic value’

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- The chair noted that application of both the ‘market size’ and ‘gross domestic product’ factors require considerations beyond those made in assessments of ‘pharmacoeconomic value’.
- Since the Working Group was primarily composed of experts in pharmacoeconomics, there may be important technical considerations for the application of these two factors that are beyond the expertise of the Working Group.

# Any questions?

Patented Medicine Prices Review Board (PMPRB)

# Questionnaire for the Steering Committee on Modernization of Price Review Process Guidelines

Due date for receiving responses: **COB April 8th, 2019**

## Topic 1: Use of external price referencing (EPR): median international price test (MIPC)

- The proposed approach is that all new medicines are assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).
- The MIPC would be recalculated annually until there are at leasdfast 7 countries or 3 years post first date of sale. At that point the MLP would no longer be interim. This approach provides both predictability (e.g., exchange rate fluctuations) and reduces regulatory burden.
- Re-benching could result in the MLP being adjusted over time.
- IMS will be used to verify international list prices however filing requirements for patentees will remain unchanged for the new schedule.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

| Stakeholder input/comments: Click or tap here to enter text. |
|---|

2. **Should exceptions be made to the MLP-MIPC test and, if so, when and why?**

| Stakeholder input/comments: Click or tap here to enter text. |
|---|

3. **Should there be a price floor for Category 2 medicines based on Lowest International Price Comparison (LIPC)?**

| Stakeholder input/comments: Click or tap here to enter text. |
|---|

4. **Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

5. **Should an increasing gap between MIPC and the MLP trigger a re- bench?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

6. **Should EPR differ depending on category or vintage of the patented medicine?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

## Topic 2: Use of List and Net Price Ceilings

- The conceptual framework presented to the SC at the first meeting proposed the establishment of two ceilings for Category 1 medicines based on both list (MLP) and net (rebated) prices (MRP).
- For Category 2 medicines, the proposal is to establish one ceiling (MLP) based on list prices domestically and internationally based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC). No Category 2 medicine will be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- The approach aims to establish a net price ceiling to both protect Canada's true transaction price from being exposed and allow patentees to comply with the net price ceilings through use of all discounts/rebates direct and indirect.

### Questions

1. **Should a Category 1 medicine ever have more than one MRP?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

2. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

3. **Should confidential third party pricing information only be used for compliance purposes?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

## Topic 3: Risk Assessment and Prioritization Criteria for Category 1 & 2 medicines

- The second part of the framework consists of a screening phase which would classify new patented medicines as either high or low priority based on their anticipated impact on Canadian consumers, including individual patients and institutional payers (e.g., public and private drug plans).
- The framework proposed high level criteria that PMPRB would use to categorize medicines as Category 1 or 2:
    - First in class or substantial improvement over existing medicines for clinically significant indication(s)
    - Market Size >Affordability Threshold
    - ICER > maximum opportunity cost threshold
    - Annual or treatment cost> per capita GDP
- Medicines that appear to be high priority based on these screening factors would be subject to automatic investigation and a comprehensive review to determine whether their price is potentially excessive.

### Questions

1. **Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

2. **Should further categories exist with different treatment modalities?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

3. **Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

4. **Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

5. **Should Category 2 medicines be scrutinized more or less than proposed?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

## Topic 4: Re-Benching Criteria

- All new medicines will be given an interim MLP of 3 years or until the medicine is sold in 7 countries, whichever comes first.
- MLP is then frozen, as is MRP, unless re-benching is triggered by one of the following criteria:
    - Approval of a new indication
    - Sales in excess of expected market size
    - New evidence on cost-effectiveness (e.g. CADTH therapeutic class review or lifting of HC conditions on NOC)
    - Significant changes in international prices (eg. MIPC < MIPC at intro by more than 25%)
- Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI
- Complaints received by the PMPRB will trigger an investigation, during which the PMPRB will assess whether:

- The medicine is in compliance with the Guidelines; and
- Whether circumstances in the market have changed to warrant a re-benching/reclassification.

### Question

1. **How often and in what circumstances should a medicine be re-benched?**

| Stakeholder input/comments:Click or tap here to enter text. |
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## Topic 5: Tests for Category 1 Medicines

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).
- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?**

| Stakeholder input/comments:Click or tap here to enter text. |
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2. **Should exceptions be made to the MIPC test and, if so, when and why?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

3. **Should the cost effectiveness threshold for Category 1 drugs vary?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

4. **Should a Category 1 medicine ever have more than one MRP?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

5. **Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

## Topic 6: Tests for Category 2 Medicines

- Category 2 medicines have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex- factory) prices, domestically and internationally.

### Questions

1. **Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

2. **Should exceptions be made to the MIPC test and, if so, when and why?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

3. **Should there be a price floor for Category 2 drugs and, if so, should it be based on LIPC?**

| Stakeholder input/comments:Click or tap here to enter text. |
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4. **Should Category 2 drugs be scrutinized more or less than proposed?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

## Topic 7: Use of Confidential Pricing Information

- Price reviews would be conducted for the following customer classes:
  - National/Provincial Retail – list price assessed against MLP
  - National Private Payer – ATP assessed against MRP
  - Provincial Public Payer – ATP assessed against MRP in each market
- ATPs are calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

### Questions

1. **Are the proposed definitions of markets and customer classes reasonable?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

2. **Is the proposal to use third-party pricing information for compliance with the MRP reasonable?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

## Topic 8: Application of New Regime to Existing Medicines

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 drugs would be re-benched later unless a complaint is received.
- All drugs within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to come into compliance.

### Questions

1. **Is the use of MIPC as an interim ceiling reasonable?**

| Stakeholder input/comments:Click or tap here to enter text. |
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2. **Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?**

| Stakeholder input/comments:Click or tap here to enter text. |
|---|

3. **Are there reasonable alternative approaches to bringing existing medicines under the new framework?**

| Stakeholder input/comments:Click or tap here to enter text. |
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## General Question

**Are there any other questions or comments that you would like to share with the SC that have not been captured above?**

| Stakeholder input/comments:Click or tap here to enter text. |
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Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# PMPRB Steering Committee on Modernization of Price Review Process Guidelines

May 13, 2019, Ottawa

Canada

# Steering Committee Final Report

Purpose:

To summarize the deliberations of the PMPRB's Steering Committee on Modernization of Price Review Process Guidelines in providing stakeholder feedback on the PMPRB proposed new framework for regulating the prices of patented medicines.

- The report has been prepared by the PMPRB staff and will be shared with the Board for its consideration prior to the publication of new draft guidelines for public consultation later this year.
- The draft report was sent to members on May 7, 2019.
- Steering Committee members to review the draft and provide feedback prior to the publication of the final report.

# Procedure and Process

- Meetings of the Steering Committee:
  - Three face-to-face meetings in Ottawa on June 25, 2018, December 13, 2018, and May 13, 2019,
  - Four teleconferences on July 24, 2018, August 15, 2018, September 12, 2018 and March 15, 2019.
- The PMPRB provided the Steering Committee with ongoing communication and regular updates throughout this consultation process, including roadmap discussions
- The PMPRB invited the Steering Committee throughout this consultation process to put forward comments, questions, and provided feedback, written and/or non-written.
- On March 20, 2019, members were asked to provide written feedback on specific questions relating to each part by April 8, 2019

# Technical Working Group

- Meetings of the Working Group:
  - Three face-to-face meetings in Ottawa: July 26, 2018, October 12, 2018, February 5, 2019,
  - Three teleconferences: August 24, 2018, September 25, 2018 and November 28, 2018. Included breakout sessions on August 22 and 24, 2018.
- The Working Group produced a Technical Report that was provided to the members of the Steering Committee in March and the Chair lead the presentation of the report and discussions with the Steering Committee on March 15 and on May 13, 2019
- The report provides a summary of the Working Group's deliberations and recommendations, around the following issues:
  - Options for determining what medicines fall into 'Category 1'
  - Application of supply-side cost effectiveness thresholds in setting ceiling prices for Category 1 medicines
  - Medicines with multiple indications
  - Accounting for uncertainty
  - Perspectives
  - Application of the market size factor in setting ceiling prices

# PMPRB Framework Modernization

- The PMPRB proposed a five-part Guidelines framework
  - Part 1: MLP based on MIPC;
  - Part II: Categorization;
  - Part III: Category 1 (MRP);
  - Part IV: Category 2 (MLP);
  - Part V: Re-benching.
- The PMPRB proposed that price reviews would be conducted for three customer classes:
  1. National Retail
  2. National Private Payer
  3. Provincial Public Payer

# Topics for Discussion and Feedback

Over the course of their deliberations, Steering Committee members discussed several topics, as summarized below:

1. Use of External Price Referencing
2. Use of List Price and Net Price Ceilings
3. Risk Assessment and Prioritization Criteria for Category 1 and 2 Medicines
4. Re-benching Criteria
5. Tests for Category 1 Medicines
6. Tests for Category 2 Medicines
7. Use of Confidential Pricing Information
8. Application of New Regime to Existing Medicines
9. Additional Questions for Consideration

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# The Steering Committee Feedback

Canada

# Topic 1: Use of external price referencing (EPR): median international price test (MIPC)

- All new medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).
- This MIPC would be interim until the medicine is sold in seven countries or three years post first date of sale.
- The MLP could be re-benched over time.

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?

- Appears to be a reasonable change (Mitch Moneo, BC Ministry of Health)
- Consistent with rationale set out in Dec 2, 2017 proposal (Owen Adams, CMA)

2. Should exceptions be made to the MLP-MIPC test and, if so, when and why?

- MIPC should only apply to new medicines. Existing medicines should be grandfathered as long as they remain within HIPC (BIOTECanada)
- In exceptional circumstances: if prices reported do not reflect current market conditions (evidence provided, centralized process, adjudicated) (Mitch Moneo, BC Ministry of Health)

# Topic 1: Use of external price referencing (EPR): median international price test (MIPC)

**Summary of feedback**

3. Should there be a price floor for Category 2 medicines based on LIPC?

- No product price should be forced below the LIPC. Allow product priced below LIPC to increase to LIPC (BIOTECanada)
- Reasonable (Owen Adams, CMA)

- No, floor would discourage market competition. (Mitch Moneo, BC Ministry of Health)

4. Does the 7 countries or 3 years approach provide the right balance […]?

- Yes, based on information presented; Noted payers' preference for certainty; Monitoring/ adjustment of variability over 3 year period (Suzanne McGurn – MOHLTC)
- Reasonable (Owen Adams, CMA)
- Reasonable (Mitch Moneo, BC Ministry of Health)

- Current approach (3 years, 5 countries) is reasonable. Removing exchange effect is important: freeze MIP (introduction or interim re-bench) – (BIOTECanada)

5. Should an increasing gap between MIPC and the MLP trigger a re-bench?

- Reasonable (Owen Adams, CMA)
- Yes (Mitch Moneo, BC Ministry of Health)

- No, MIPC and MLP gaps can be temporary (then difficult to raise price) – (BIOTECanada)

6. Should EPR differ depending on category or vintage of the patented medicine?

- The EPR could be adjusted to accommodate significant price differentials with respect to vintage ….to mitigate shock to the market (Mitch Moneo, BC Ministry of Health)

- Limit existing patented medicines to HIPC, new medicines held to current guideline tests (BIOTECanada)

# Topic 2:
# Use of List Price and Net Price Ceilings (MLP, MRP)

- Category 1 medicines would have two ceilings: one based on list price (MLP) and one based on net (rebated) price (MRP).
- Category 2 medicines would have one ceiling price (MLP) based on the lower of the average domestic Therapeutic Class Comparison test and the MIPC test. No Category 2 medicine would have an MLP that is lower than the lowest country in the PMPRB12.

1. Should a Category 1 medicine ever have more than one MRP?

- Different MRP for multiple indications is problematic. MRP price threshold is inappropriate because PMPRB regulates at ex-factory price level (BIOTECanada)
- Tech WG recommended single ceiling (no basis to disagree) (Owen Adams, CMA)
- No, administratively difficult - use lowest price for all PTs (Mitch Moneo, BC MOH)

2. Are there economic considerations that would support a higher MRP for some Category 1 medicines […]?

- Consideration if exceptional circumstances (prices do not reflect market) and evidence presented through centralized process and adjudicated (Mitch Moneo, BC Ministry of Health)

- Concept of MRP should be abandoned. Market size should only consider incremental cost impact to the health care system (BIOTECanada)

3. Should confidential third party pricing information only be used for compliance purposes?

- Expects this will be a start (Owen Adams, CMA)
- If confidential pricing information is available, it should be applied to all pricing assessments (Mitch Moneo, BC Ministry of Health)

- Not used except voluntarily (e.g. at a hearing) – (BIOTECanada)

# Topic 3: Risk Assessment and Prioritization Criteria for Category 1 and 2 Medicines

- New medicines would be categorised as Category 1 or 2 based on their anticipated impact to Canadian consumers.
- Categorization criteria would take into consideration: Therapeutic alternatives, Market size, Opportunity cost, Annual/treatment cost
- Category 1 medicines would be subject to a comprehensive review to determine if the price is excessive.

1. Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?

- Reasonable. Clear definition of concepts is required (Suzanne McGurn – MOHLTC)
- Reasonable (Owen Adams, CMA)
- Reasonable. Further considerations can be made once impact is evaluated (Mitch Moneo, BC Ministry of Health)

- No. Presupposes risk-based approach is appropriate (BIOTECanada

2. Should further categories exist with different treatment modalities?

- Yes, based on an on-going assessment of the market conditions/dynamics, other categories/modalities should be considered to achieve best value (Mitch Moneo, BC Ministry of Health)

- No, risk-based approach is flawed (BIOTECanada)

- None to suggest (Owen Adams, CMA)

# Topic 3: Risk Assessment and Prioritization Criteria for Category 1 and 2 medicines

**Summary of feedback (cont'd)**

3. Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?

- Rapid changes to technology and market, so should be continuously maintained and updated (standard practice/evidence and maintained by experts) – (Mitch Moneo, BC Ministry of Health)

- Need to return to level of improvement for categorization, if necessary at all (BIOTECanada)
- Tech WG voted not to recommend additional criteria – hence agrees (Owen Adams, CMA)

4. Should the PE, market size and GDP factors apply both as screens and thresholds?

- Tech WG voted in favour of thresholds for each – hence agrees (Owen Adams, CMA)
- Both PE & market size should apply as screens and thresholds (effectiveness and utility); GDP factor is unnecessary (Mitch Moneo, BC Ministry of Health)

- Should not be used either as screen or thresholds; If applied, market size & GDP should only apply as a screen; PE factors should not be used as either (only for hearings) – (BIOTECanada)
- Pharmacoeconomics should not be the only determinant of price. The setting of a universal cost-per-QALY threshold for all medicines is not appropriate (Durhane Wong-Rieger, CORD)

5. Should Category 2 medicines be scrutinized more or less than proposed?

- Less. HIPC rule only (BIOTECanada)
- Ongoing price review or regulated price decrease for medicines on the market for a long time (i.e. 3 to 5 years) unless financial harm/impact on business viability or unable to supply medicines (Mitch Moneo, BC Ministry of Health)

# Topic 4: Re-Benching Criteria

- Approval of a new indication
- Sales in excess of expected market size
- New evidence of cost effectiveness
- Significant changes to international prices
- Application by the patentee for a re-bench with evidence of increased cost effectiveness, smaller market, or a significant increase in CPI

1. How often and in what circumstances should a medicine be re-benched?

- Triggering circumstances outlined seem reasonable – on an as-needed basis (Suzanne McGurn, MOHLTC)
- Circumstances outlined seem reasonable (i.e. as needed) – (Owen Adams, CMA)
- Criteria as set out (Mitch Moneo, BC Ministry of Health)

- Re-benching for new indications should not be implemented. Manufacturers require certainty, so to the extent re-benching is appropriate (predictable and reasonable) (BIOTECanada)

# Topic 5: Tests for Category 1 Medicines

**Summary of feedback**

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).
- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?
2. Should exceptions be made to the MIPC test and, if so, when and why?
3. Should the cost effectiveness threshold for Category 1 medicines vary?

**Responses in line with the those in Topic 1**

- Agrees with Technical WG: further empirical research (Owen Adams, CMA)

- No, the most cost effective amount should be applied consistently for the category. Exceptional cases can be re-assessed (as required) – (Mitch Moneo, BC Ministry of Health)

4. Should a Category 1 medicine ever have more than one MRP?

- Tech WG recommended single (no basis to disagree) (Owen Adams, CMA)
- No, too difficult to manage/administer different prices across PTs (goal is to establish a best price for all PTs) – (Mitch Moneo, BC Ministry of Health)

5. Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?

- Consideration for only exceptional situations – evidence provided and validated by a standardized process (Mitch Moneo, BC Ministry of Health)

# Topic 6: Tests for Category 2 Medicines

## Summary of feedback

- Category 2 medicines would have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class.
- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex-factory) prices, domestically and internationally.

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?

- Reasonable – Topic 1, Q1 (Owen Adams, CMA)
- Reasonable (Mitch Moneo, BC Ministry of Health)

2. Should exceptions be made to the MIPC test and, if so, when and why?

- No (Mitch Moneo, BC Ministry of Health)

3. Should there be a price floor for Category 2 drugs and, if so, should it be based on LIPC?

- Reasonable – Topic 1, Q3 (Owen Adams, CMA)
- No floor price is preferable however the LIPC approach is reasonable (Mitch Moneo, BC Ministry of Health)

4. Should Category 2 drugs be scrutinized more or less than proposed?

- Category 2 drugs should be scrutinized regularly. If on the formulary > 5 years consider statutory price reductions as occurs in other jurisdictions (Mitch Moneo, BC Ministry of Health)

# Topic 7: Use of Confidential Pricing Information

- Price reviews would be conducted for the following customer classes:
  a. National/Provincial Retail – list price assessed against MLP
  b. National Private Payer – ATP assessed against MRP
  c. Provincial Public Payer – ATP assessed against MRP in each market
- ATPs would be calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

1. Are the proposed definitions of markets and customer classes reasonable?

- Yes, if confidential pricing information is available (Mitch Moneo, BC Ministry of Health)

- Wonder if you need to distinguish between public drug programs and public hospital drug purchasing (Owen Adams, CMA)

2. Is the proposal to use third-party pricing information for compliance with the MRP reasonable?

- Assuming that it is feasible to accurately compile this information (Owen Adams, CMA)
- Yes, if confidential pricing information is available (Mitch Moneo, BC Ministry of Health)

# Topic 8: Application of New Regime to Existing Medicines

## Summary of feedback

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 medicines would be re-benched later unless a complaint is received.
- All medicines within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to address the issue.

1. Is the use of MIPC as an interim ceiling reasonable?

- Reasonable (Owen Adams, CMA)
- Yes (Mitch Moneo, BC Ministry of Health)

2. Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?

- Perhaps only Category 1 (Owen Adams, CMA)
- Yes (could consider a transition period to allow for business adjustments) – (Mitch Moneo, BC Ministry of Health)

3. Are there reasonable alternative approaches to bringing existing medicines under the new framework?

- None noted (Owen Adams, CMA)
- As above (Mitch Moneo, BC Ministry of Health)

# General statements made by the Steering Committee members

- "I am writing on behalf of the life and health insurance industry to indicate our continued strong support for the modernization framework for the Patented Medicine Prices Review Board". (CLHIA, April 16, 2019)
- BC fully supports the modernization efforts and appreciates all the work that has been accomplished as an important step towards ensuring drug prices are not excessive and the sustainability of public drug plans (Mitch Moneo, BC Ministry of Health)
- The proposed framework strikes an appropriate balance… conducive to innovation in the pharmaceutical industry, while controlling the costs of prescription drugs. It is crucial that the government move ahead with the PMPRB modernization framework.

- "IMC continues to have serious policy and process concerns about the proposed amendments, and reserves its right to oppose the proposed amendments and the work of the Steering Committee and Working Group to the extent it is intended to implement or reflect the proposed amendments." (IMC, July 13, 2018)
- "It is the BMC's position that if there is not sufficient clarity on impact on patient care and on system efficiency, value and sustainability reforms must be halted until there is full certainty." (BMC, February 14, 2018)
- "We are concerned about (the) government's proposed changes to the Patented Medicines Regulations, which would overhaul how the Patented Medicine Prices Review Board (PMPRB) sets maximum (non-excessive) prices for patented drugs in Canada." (CORD and Myeloma Canada, April 8, 2019)

# Final Report and Next Steps

- The final report will be published following the feedback received on the draft
- Board staff will present analysis of consultation, along with SC and TWG report to Board for consideration
- Feedback will be part of the considerations in developing draft set of Guidelines which will be consulted on more broadly post publication of CG2

Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

# THANK YOU

**Patented Medicine Prices Review Board**

Canada

The first meeting of the PMPRB Steering Committee on Modernization of Price Review Process Guidelines was held June 25, 2018 in Ottawa.

The Terms of Reference were agreed upon by all members present. PMPRB clarified that the term "respective organizations" in the Confidentiality section included, as applicable, companies who are members of the Steering Committee association, and advisors to the members. IMC noted for the record that, although it will attempt to participate constructively in the process, it is opposed to many of the proposed regulatory changes to the *Patented Medicines Regulations*, and that its participation in the Steering Committee did not imply support for the aforementioned proposed changes.

Members discussed the proposed timelines for implementation of the changes to the Regulations and the PMPRB's development of Guidelines. Several members expressed the view that the PMPRB's consultations were premature before CG2 publication. Board Staff responded that January 1, 2019 remains the implementation date until the Minister of Health directs otherwise, but that any changes resulting from the CG2 process would necessarily be addressed before the issuance of draft Guidelines for additional consultation.

Board Staff presented the proposed PMPRB framework modernization structure for discussion by members. Discussion focused on the potential impact of the proposed framework on patient access to new and existing medicines; the interface between the PMPRB, health technology assessment agencies, and the pCPA; and the PMPRB's proposed use of pharmacoeconomic value in price review.

A list of suggested questions related to the framework was proposed to the Steering Committee to encourage targeted feedback; it was agreed that this list may expand as the Steering Committee considers appropriate. A Technical working group will be formed to answer specific economic and clinical questions, and additional working groups to address specific topics may be considered by the Committee as needed. The Steering Committee's next meeting will be scheduled in July.

Minutes of Steering Committee Meeting, July 24, 2018 1:00 pm teleconference

The PMPRB Steering Committee on Modernization of Price Review Process Guidelines met via teleconference on July 24, 2018.

The draft minutes from last meeting were tentatively approved pending the posting of suggested modifications by IMC.

PMPRB Staff provided an update on changes to the Terms of Reference for the technical Working Group. In response to a specific request from the members representing BioteCanada, PMPRB Staff also presented a consultation "Roadmap" which identified the dates of future Steering Committee meetings and the topics to be discussed at each such meeting.

Members also discussed the process for providing feedback on Steering Committee deliberations via written submissions. It was agreed that at the end of each meeting, the co-chairs will endeavour to summarise the relevant questions that arose over the course of the discussion and invite members to provide any written feedback on those questions no later than 3 working days before the next meeting. A synopsis of the feedback received and the PMPRB's response to any outstanding issues or questions raised by members in their submissions will be provided by the co-chairs at the beginning of each subsequent meeting.

The next Steering Committee meeting will be held in mid-August. Members will be contacted shortly to confirm availability for the next meeting. Members will also discuss submissions received to date regarding the scope of issues the Committee will consider and whether additional Working Groups are appropriate.

# SUMMARY

**PMPRB Steering Committee on Modernization of Price Review Process Guidelines**
**August 15, 2018**
**Ottawa**
**11:00 a.m. to 4:00 p.m. EDT**

*Participants:* Suzanne McGurn (MHLTC and CADTH), Mitch Moneo (BC and CADTH), Dr. Robin McLeod (Cancer Care Ontario), Sylvie Bouchard (INESSS), Pamela Fralick (IMC), Laurene Redding (AstraZeneca and BioteCanada), Durhane Wong-Rieger (CORD), Dr. Jeff Blackmer (CMA), Glen Doucet (CPhA), Jody Cox (CGPA and Biosimilars Canada), Stephen Frank (CLHIA)

*Observers:* Karen Reynolds (Health Canada), Nelson Millar (Health Canada), Georgina Georgilopoulos (ISED), Declan Hamill (IMC), Paul Petrelli (Jazz and BioteCanada)

*PMPRB:* Tanya Potashnik, Matthew Kellison, Guillaume Couillard, Theresa Morrison

The PMPRB Steering Committee on Modernization of Price Review Process Guidelines met via teleconference on August 15, 2018. The draft minutes from the July 24, 2018 meeting were tentatively approved, with members having until the end of August 16, 2018 to suggest any further modifications.

Board Staff summarised the first meeting of the Technical Working Group (TWG). A draft summary from this meeting was provided to Steering Committee members for information. It was recognised that it may change following feedback from the TWG members.

Written feedback received by the PMPRB was shared with the group. Written feedback that is beyond scope of Steering Committee Terms of Reference will be included as annex to the final Steering Committee report.

Board Staff summarised the proposed PMPRB framework modernization structure presented to members during the first Steering Committee meeting. Members then discussed four topics designed to elicit specific feedback on areas of focus. Each member may choose to submit written feedback on these topics up to three days before the next meeting.

Topic 1: Use of External Price Referencing (EPR) Part 1: Median International Price Test (MIPC)

Board Staff presented the proposed use of EPR:

- All new medicines are assigned a Maximum List Price (MLP) based on the median of the PMPRB12 (MIPC).
- This MIPC would be interim until the medicine is sold in seven countries or three years post first date of sale.
- The MLP could be re-benched over time.

Members were asked the following questions:

1. Is an MLP based on the median of PMPRB12 (MIPC) for all medicines reasonable?
2. Should exceptions be made to the MLP-MIPC test and, if so, when and why?
3. Should there be a price floor for Category 2 medicines based on Lowest International Price (LIPC)?
4. Does the 7 countries or 3 years approach provide the right balance of reflecting international prices and providing stakeholders with reasonable predictability?
5. Should an increasing gap between the MIPC and the MLP trigger a re-bench?
6. Should EPR differ depending on the category or vintage of the patented medicine?

Members briefly discussed how medicines only sold in the US would be reviewed. Members representing the pharmaceutical industry were concerned the LIPC floor would increase uncertainty given it could change with each additional country launch. Some members believed it would be useful for Board Staff to share the sources it uses to independently verify the international prices filed by patentees. Some members voiced concern that this approach would not work for biosimilar medicines. Members expressed that examples would facilitate discussion on this point. Several members preferred to provide input via written submission.

Topic 2: Use of List and Net Price Ceilings (MLP, MRP)

Board Staff reviewed the proposed framework previously presented to the Steering Committee.

- Category 1 medicines will have two ceilings: one based on list price (MLP) and one based on net (rebated) price (MRP).
- Category 2 medicines will have one ceiling price (MLP) based on the lower of the average domestic Therapeutic Class Comparison (TCC) test and the MIPC test. No Category 2 medicine will have an MLP that is lower than the lowest country in the PMPRB12.

Members were asked the following questions:

1. Should a Category 1 medicine ever have more than one MRP?
2. Are there economic considerations that would support a higher MRP for some Category 1 medicines that would result from the proposed application of the new factors?
3. Should confidential third party pricing information only be used for compliance purposes?

Members expressed the importance of developing a flexible system that is adaptable to future challenges in an environment where medicines are increasingly individualised. Several members preferred to provide input via written submission.

Topic 3: Risk Assessment and Prioritization Criteria for Category 1 & 2 medicines

Board Staff reviewed the proposed classification criteria previously presented to the Steering Committee.

- New medicines would be categorised as Category 1 or 2 based on their anticipated impact to Canadian consumers.
- Categorization criteria would take into consideration:
    - Therapeutic alternatives
    - Market size
    - Opportunity cost
    - Annual/treatment cost
- Category 1 medicines would be subject to a comprehensive review to determine if the price is excessive.

Members were asked the following questions:

1. Is the proposed division and treatment of Category 1 and Category 2 medicines a reasonable risk-based regulatory approach?
2. Should further categories exist with differential treatment modalities?
3. Should more or less criteria be considered in screening a medicine as higher risk and where should the line be drawn with respect to the criteria?
4. Should the pharmacoeconomic, market size and GDP factors apply both as screens and thresholds?
5. Should Category 2 medicines be scrutinized more or less than proposed?

The PMPRB agreed to share analysis that models the impact of using different threshold parameters for each of the categorisation criteria. Members discussed the extent to which payers have the tools to negotiate the price of medicines with therapeutic comparators; i.e. line extensions and generic products, and whether an MRP would be useful for a Category 2 medicine. Some members expressed that disclosing an MRP for Category 1 medicines would facilitate price negotiations with payers. Several members preferred to provide input via written submission.

Topic 4: Re-Benching Criteria

Board Staff reviewed the proposed re-benching criteria previously presented to the Steering Committee.

- Approval of a new indication
- Sales in excess of expected market size
- New evidence of cost effectiveness
- Significant changes to international prices
- Application by the patentee for a re-bench with evidence of increased cost effectiveness, smaller market, or a significant increase in CPI

Members were asked the following questions:

1. How often and in what circumstances should a medicine be re-benched?

Members discussed the potential difficulty, from an industry perspective, with determining the market size prospectively, for a medicine that treats a new therapeutic area. The need to have

clear definitions of the re-benching criteria was expressed. As well, the concern was raised that automatic re-benching of medicines following a specific time interval may introduce uncertainty for both patentees and patients.

The role of the Steering Committee and need for additional working groups was discussed. PMPRB staff indicated that the Committee's role is to analyze the framework proposed by the PMPRB and consider its feasibility. Issues outside the scope of the proposed framework, or alternative frameworks, can be submitted by members to be included as an annex in the Committee's report. PMPRB staff recommended focusing any additional working groups at this time on specific high-level framework topics that are not currently addressed by the Steering Committee. It was recommended that all other issues, i.e. operational challenges, may be better suited to working groups later in the Guideline development process. Some members expressed the preference of dealing with these smaller issues earlier in the process.

The next Steering Committee meeting will take place in early September. PMPRB will summarize written submissions received from members in advance of the meeting and lead discussions surrounding the following themes:

1. Tests for Category 1 medicines
2. Tests for Category 2 medicines
3. Use of confidential pricing information
4. Application of new regime to existing medicines.

# SUMMARY

**PMPRB Steering Committee on Modernization of Price Review Process Guidelines**
**September 12, 2018**
**Ottawa**
**11:00 a.m. to 1:00 p.m. EDT**

*Participants:* Mitch Moneo (BC and CADTH), Scott Doidge (NIHB), Chander Sehgal (IMC), Laurene Redding (AstraZeneca and BioteCanada), Durhane Wong-Rieger (CORD), Owen Adams (CMA), Glen Doucet (CPhA), Jody Cox (CGPA and Biosimilars Canada), Stephen Frank (CLHIA), Paulette Eddy (Best Medicines Coalition), Martine Elias (Myeloma Canada)

*Observers:* Karen Reynolds (Health Canada), Rodrigo Arancibia (ISED), Michael Dietrich (IMC)

*PMPRB:* Doug Clark, Tanya Potashnik, Matthew Kellison, Guillaume Couillard, Isabel Jaen Raasch, Richard Lemay, Theresa Morrison

The third meeting of the PMPRB Steering Committee on Modernization of Price Review Process Guidelines took place via teleconference on September 12, 2018. The draft minutes from the August 15, 2018 meeting were approved.

Board Staff summarised the breakout sessions of the Technical Working Group (TWG). A summary of these meetings will be provided to Steering Committee members for information once a final version is available. The final report of the TWG will be shared with the Steering Committee during the October meeting.

Members discussed that the final draft of Dr. David Dodge's independent assessment of Health Canada's cost-benefit analysis of the proposed amendments had been provided to IMC and BioteCanada by Health Canada. The observer from Health Canada agreed to provide the draft report to other Steering Committee members.

Board Staff summarised the proposed PMPRB framework modernization structure presented to members during the first Steering Committee meeting. Members were presented four topics designed to elicit specific feedback. Clarifying questions were answered by Board Staff and Steering Committee members will provide written feedback in response to the questions. Written feedback that is beyond scope of Steering Committee Terms of Reference will be included as annex to the final Steering Committee report.

Topic 1: Tests for Category 1 Medicines

Board Staff presented the following tests for Category 1 medicines:

- Category 1 medicines would be assigned a Maximum List Price (MLP) based on the median of the PMPRB12 basket (MIPC).
- Category 1 medicines would subsequently be given a Maximum Rebated Price (MRP).

- The MRP would be based on application of the pharmacoeconomic, market size, and GDP factors.

Members were asked the following questions:

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all medicines reasonable?
2. Should exceptions be made to the MIPC test and, if so, when and why?
3. Should the cost effectiveness threshold for Category 1 drugs vary?
4. Should a Category 1 medicine ever have more than one MRP?
5. Are there economic considerations that would support a higher MRP for some Category 1 medicines than would result from the proposed application of the new factors?

Members will provide input via written submission.

Topic 2: Tests for Category 2 Medicines

Board Staff reviewed the proposed tests for Category 2 medicines.

- Category 2 medicines have an MLP based on the lower of the MIPC and the average of the domestic therapeutic class (ATCC).
- However, no Category 2 medicines would be given an MLP that is lower than the lowest price country in the PMPRB12 (LIPC floor).
- An MRP would not be established for Category 2 medicines.
- The MLP would be established based on publicly available list (ex-factory) prices, domestically and internationally.

Members were asked the following questions:

1. Is an MLP based on the median of the PMPRB12 (MIPC) for all drugs reasonable?
1. Should exceptions be made to the MIPC test and, if so, when and why?
2. Should there be a price floor for Category 2 drugs and, if so, should it be based on LIPC?
3. Should Category 2 drugs be scrutinized more or less than proposed?

Members will provide input via written submission.

Topic 3: Use of Confidential Pricing Information

Board Staff reviewed the proposed ways in which confidential pricing information may be considered.

- Price reviews would be conducted for the following customer classes:
    a. National/Provincial Retail – list price assessed against MLP
    b. National Private Payer – ATP assessed against MRP
    c. Provincial Public Payer – ATP assessed against MRP in each market
- ATPs are calculated net of all direct and indirect discounts and benefits.
- Category 2 medicines would be assessed against MLP only.

Members were asked the following questions:

1. Are the proposed definitions of markets and customer classes reasonable?
2. Is the proposal to use third-party pricing information for compliance with the MRP reasonable?
3. Other questions proposed by Steering Committee members?

One member expressed concern that patentees might have difficulty tracing ex-factory sales to the end user in order to provide the PMPRB with a medicine-level breakdown of specific benefits given to public or private payers. The PMPRB acknowledged that a further working group would need to examine this issue during subsequent consultations.

Members will provide input via written submission.

Topic 4: Application of New Regime to Existing Medicines

Board Staff reviewed the proposed method of applying new Guidelines to existing medicines.

- Existing medicines would be given an interim price ceiling based on the lower of their current ceiling and the MIPC of the PMPRB12.
- Existing medicines would only be classified as Category 1 if they do not meet a $100K/QALY screen for any indication. These would be prioritized for re-benching and subject to the same methodology proposed for new Category 1 medicines.
- Category 2 drugs would be re-benched later unless a complaint is received.
- All drugs within a therapeutic class would be assessed at the same time for the purposes of the ATCC test.
- Patentees would be advised in advance of re-benching and given two reporting periods to come into compliance.

Members were asked the following questions:

1. Is the use of MIPC as an interim ceiling reasonable?
2. Should existing medicines be subject to a Category 1 or 2 classification and re-benched on this basis?
3. Are there reasonable alternative approaches to bringing existing medicines under the new framework?
4. Other questions proposed by Steering Committee members?

Members will provide input via written submission.

Additional Questions for Consideration

Board Staff posed the following additional questions to members for consideration:

1. Are there opportunities to further reduce regulatory burden while still operationalizing the new factors?
2. Other questions proposed by Steering Committee members?

Members will provide input via written submission.

The next Steering Committee meeting will take place in October. The PMPRB will present hypothetical case studies to demonstrate how medicines would be evaluated using the proposed framework. Time will be allocated for members to discuss the questions posed to the Steering Committee. The Chair of the TWG will be in attendance to present the findings of the group and respond to questions from the Steering Committee.

# SUMMARY

**PMPRB Steering Committee on Modernization of Price Review Process Guidelines**
**December 13, 2018**
**Ottawa, The Alt**
**9:30 a.m. to 4:00 p.m. EST**

*Participants:* Suzanne McGurn (MHLTC and CADTH), Mitch Moneo (BC and CADTH), Susan Pierce (NIHB), Dr. Robin McLeod (Cancer Care Ontario), Brent Fraser (CADTH), Sylvie Bouchard (INESS), Patrick Dufort (INESS), Stephen Frank (CLHIA), Pamela Fralik (IMC), Laurene Redding (AstraZeneca and BioteCanada), Durhane Wong-Rieger (CORD), Owen Adams (CMA), Gail Attara (GI Society, Best Medicines Coalition), Martine Elias (Myeloma Canada)

*Observers:* Karen Reynolds (Health Canada), Rodrigo Arancibia (ISED), Declan Hamill (IMC) Paul Petrelli (Jazz Pharmaceuticals, BioteCanada)

*PMPRB:* Dr. Mitch Levine (opening of meeting only), Tanya Potashnik, Matthew Kellison, Guillaume Couillard, Isabel Jaen Raasch, Marie-Eve St-Hilaire, Thy Dinh, Theresa Morrison

The fourth meeting of the PMPRB Steering Committee on Modernization of Price Review Process Guidelines took place on December 13, 2018.

The Chairperson of the Board opened the meeting with a re-review of the rationale for the Steering Committee. He reiterated that there will continue to be opportunities for Stakeholders to consult on the draft Guidelines once they are made public.

Board Staff summarized the progress to date of the Technical Working Group (TWG). The final draft report of the TWG will be shared with the Steering Committee when available, at the end of February 2019.

Case studies and background documents had been shared by the PMPRB with members prior to the meeting. Additionally, members representing BIOTECanada had developed and circulated case studies for consideration. The PMPRB presented its hypothetical case studies to demonstrate how medicines would be evaluated using the proposed framework. The outcomes of the current Guidelines versus the proposed Guidelines were compared and contrasted. Clarifying questions were answered by Board Staff.

<u>Case 1: Large Population, with existing therapeutic comparators</u>

Board Staff presented the following case study. A medicine that:

- Treats a chronic condition
- Has therapeutic comparators
- Has one approved indication
- Has an annual treatment cost of $1,000

- Has a very large potential treatment population: 500,000 patients
- Has potential annual revenues of $500,000,000
- Triggers the proposed market size threshold to be considered a Category 1 medicine

Board Staff explained the application of the proposed Guidelines, highlighting changes in the MLP and MRP over time based on the MIPC and market size (based on actual revenues) in years 2 and 3. Members representing the pharmaceutical industry expressed concern that there might be a disincentive to be the first to launch a new medicine. Members representing patients were concerned that decreased MRP due to increased market size might encourage decreased access to patients during the introductory period. Other members felt that the realties of the market would override these concerns. A member representing public payers expressed that if the proposed framework resulted in closer starting points for price negotiations, negotiations could be quicker and easier and patients could access medicines faster.

Case 2: Large Population, with no therapeutic alternatives

Board Staff presented the following case study. A medicine that:

- Treats a chronic condition
- Has no therapeutic comparators
- Has one clinically significant approved indication
- Has an annual treatment cost of $7,000
- Has a large potential treatment population: 100,000 patients
- Has potential annual revenues of $700,000,000
- Is a Category 1 medicine based on market size and lack of therapeutic comparators

Board Staff explained the application of the proposed Guidelines, highlighting that the MRP was established by setting a ceiling based on the pharmacoeconomic value threshold and then adjusting that ceiling down based on market size. It was explained that the MRP will not be published by Board Staff but could be shared with payers by patentees. A member representing private payers questioned how useful a confidential MRP would be to private payers. A member representing pharmaceutical companies reiterated their position that it is not possible to accurately report on benefits given to private payers.

Case 3: Two indications with different therapeutic benefits and prevalence rates

Board Staff presented the following case study. A medicine that:

- Treats 2 chronic conditions
    - Condition 1 (first indication):
        - potential patient population: 3,000
        - no therapeutic alternative and offers significant therapeutic improvement over standard of care
    - Condition 2 (second indication):
        - potential patient population: 100,000
        - no therapeutic improvement over therapeutic alternatives

- Has an annual treatment cost of $20,000
- Has potential annual revenues of $2B

- Is a Category 1 medicine based on market size

Board Staff explained the application of the proposed Guidelines, highlighting the different MLP and MRP calculations for the first and second indication. It was discussed that having two indications at launch is not as likely as having one approved indication shortly followed by subsequent indications, and members felt it would be useful to explore this scenario in more detail. Board Staff indicated that a new indication would be a trigger to revisit the MRP. One member suggested the use of revenue increases as the trigger to a re-bench instead of subsequent approved indications. It was also mentioned that setting an indication-specific price would be challenging to implement. Finally, Board Staff confirmed that the MRP could increase if the result of the review warrant a higher ceiling.

Case 4: 2nd line oncology medicine

Board Staff presented the following case study. A medicine that:

- Has several therapeutic comparators
- Has one clinically significant approved indication
- Has an annual treatment cost of $50,000
- Has a small potential treatment population with low 5-year survival rates: 3,000 patients
- Has potential annual revenues of $150,000,000
- Is a Category 1 medicine based on market size and annual treatment cost above GDP/capita

Board Staff explained the application of the proposed Guidelines, highlighting that the MRP was established by setting a ceiling based on the pharmacoeconomic value threshold and then adjusting that ceiling up based on small market size. One member suggested a case study that specifically evaluates the complexity of oncology medicines that have multiple indications that are introduced sequentially and in combination with other medicines would be useful.

Case 5: Curable condition, large treatment population

Board Staff presented the following case study. A medicine that:

- Is a cure for a common and serious condition
- Has an annual treatment cost of $50,000
- Has a large potential treatment population: 200,000 patients
- Has potential annual revenues of $1.5B
- Is a Category 1 medicine based on market size and annual treatment cost above GDP/capita

Board Staff explained the application of the proposed Guidelines, highlighting that the MRP was established by setting a ceiling based on the pharmacoeconomic value threshold and then adjusting that ceiling down based on market size. In this example the price was already below the cost effective price determined by pharmacoeconomic analysis, but the large market size required an additional price reduction.

Case 6: Rare disease drug

Board Staff presented the following case study. A medicine that:

- Offers a moderate improvement over placebo for a severe condition with high burden of illness and high unmet need
- Has one indication
- Has an annual treatment cost of $300,000
- Has a small potential treatment population: 1,000 patients (increasing 2% annually)
- Has potential annual revenues of $300,000,000
- Is a Category 1 medicine based on market size and annual treatment cost above GDP/capita

Board Staff explained the application of the proposed Guidelines, highlighting that the MRP was established by setting a ceiling based on the pharmacoeconomic value threshold and then adjusting that ceiling up based on small market size . Board Staff noted that the factor of increase will be determine by consultation. It was mentioned that expenses associated with the cost of care, infusion clinics, helping with cost of care, etc. are all expenses that the company could argue be included in the net revenue calculation of the medicine.

Following the presentation of the case studies, members had an open discussion. It was suggested that re-benching case studies would be useful to get an idea of the impact to medicines that are currently on the market. Members representing patient groups voiced the concern that price reductions may have a widespread impact on research and development, access to clinical trials and access to medicines in Canada. Members representing payers explained that as prices rise, even the status quo impacts patient access and this will only continue.

Members representing BIOTECanada indicated their intent to revise the case studies they had previously prepared for discussion to take the same approach as the PMPRB case studies before presenting them to the group in order to facilitate discussion.

The TWG report will be available to share the first week in March 2019. An email will be sent to members with questions and seeking formal feedback which will be complied into one report. The next Steering Committee meeting will take place in early April to go over the draft report. The Chair of the TWG will be in attendance to present the findings of the group and respond to questions from the Steering Committee.

# SUMMARY

**PMPRB Steering Committee on Modernization of Price Review Process Guidelines**
**May 13, 2019**
**Ottawa, The Alt**
**9:30 a.m. to 4:00 p.m. EST**

*Participants:* Suzanne McGurn (MHLTC and CADTH), Mitch Moneo (BC and CADTH), Susan Pierce (NIHB), Brian O'Rourke (CADTH), Sylvie Bouchard (INESSS), Karen Voin (CLHIA), Pamela Fralick (IMC), Laurene Redding (AstraZeneca and BioteCanada), Durhane Wong-Rieger (CORD), Owen Adams (CMA), Joelle Walker (Canadian Pharmacists Association), Paulette Eddy (GI Society, Best Medicines Coalition), Martine Elias (Myeloma Canada)

*Observers:* Karen Reynolds (Health Canada), Benoit Leduc (ISED), Declan Hamill (IMC), Paul Petrelli (Jazz Pharmaceuticals, BioteCanada)

*PMPRB:* Tanya Potashnik, Matthew Kellison, Isabel Jaen Raasch, Marie-Eve St-Hilaire, Elena Lungu, Theresa Morrison

The final meeting of the PMPRB Steering Committee on Modernization of Price Review Process Guidelines took place on May 13, 2019.

The co-chairs of the Steering Committee opened the meeting. The objectives of the meeting were to present the final report of the Technical Working Group (TWG) and subsequently to discuss of the draft final report of the Steering Committee.

The report of the TWG was first presented to Steering Committee members in March 2019. Feedback from members following that presentation suggested that the Steering Committee would benefit from additional discussion of the TWG report. Accordingly, the TWG Chair, Dr. Mike Paulden, and two members of the TWG, Dr. Chris McCabe and Dr. Stuart Peacock, presented the TWG report, responded to technical questions and provided additional insight into the group's deliberations.

Some members expressed concern that the scope of the TWG was too narrow and failed to take into consideration approaches for operationalizing the proposed new regulations other than what was laid out in the proposed framework.

Some members raised concern that using pharmacoeconomic models in setting the ceiling price of a medicine decreases transparency for third parties because the model, inputs and assumptions are all confidential. Board staff agreed that further exploration around information sharing and transparency with CADTH and INESSS would be required as the operational framework is finalized.

Members recommended the need to implement a change management plan to evaluate the success of the new regulatory framework going forward and to adjust the framework based on

real world evidence. Board Staff agreed that a transparent evaluation plan should be put in place and reported on annually.

Board Staff presented the draft Steering Committee report and noted that the report did not make specific recommendations as that was not part of the Steering Committee's Terms of Reference. Additionally not all members responded to the questions posed on the proposed framework, so it was not possible to determine points of agreement. Some members felt that it would be appropriate to include a more detailed summary of all feedback received for each question posed to the Steering Committee in the body of the report, and/or an executive summary.

Some members expressed concerns that the substance of individual feedback would not be adequately communicated to the Board given its position in the report's appendices. It was suggested individual feedback be given a more prominent place in the report.

Some members also suggested that the report should carry a disclaimer or short summary noting the inherent challenges of the Steering Committee's work and the key themes of concern. It was also suggested that the next steps in in the process should be laid out in the report, including relevant timelines.

Members representing BIOTECanada had previously developed case studies for consideration. They were revised to reflect the same approach as was taken in the PMPRB's previous case studies. It was agreed these case studies would be circulated to the membership.

Board staff agreed that additional written feedback on the content of the draft report could be provided until May 17, 2019 for consideration in the final report. The final report will be provided to Steering Committee members by the end of May 2019 in advance of its presentation to Board Members for consideration. The report will subsequently be made public on the PMPRB website, along with details on the PMPRB's forthcoming consultations on draft Guidelines.

Board Staff thanked the Steering Committee members for their participation.

“While IMC is committed to constructive engagement with the PMPRB on Modernization of Price Review Process Guidelines, our participation on the Steering Committee and the Working Group should not be interpreted as supporting the proposed amendments to the Regulations.”