Patented
Medicine Prices
Review Board

PMPRB NEWSletter

Volume 9, Issue No. 3
July 2005

Inside...

Since our last issue...

Here are some of the key events that occurred since the end of April 2005.

April 28:	Réal Sureau participated in the Administrative Tribunal Member's Forum 2005 – *Update on latest trends in Administrative Law*, in Ottawa.
June 14:	The PMPRB 2004 Annual Report was tabled before Parliament.
June 15-19:	The PMPRB celebrated the National Public Service Week 2005.
June 19-21:	Réal Sureau, Barbara Ouellet, Martine Richard and Sylvie Dupont attended the Canadian Council of Administrative Tribunals (CCAT) Annual Conference, in Ottawa. ■

Comings and Goings

- Dr. Brien Benoit was appointed Member of the PMPRB in May, and Vice-Chairperson designate as of October 3, 2005, for a 5-year term. Dr. Benoit's biographical notes are available on our Web site under "About the PMPRB"; "Membership".
- Orlando Manti, who had been on secondment with Health Canada, rejoined the PMPRB as Senior Economist, with the Policy and Economic Branch. Welcome back!
- Best wishes to Louis-Philippe Dubrule who has accepted a position with the Treasury Board Secretariat.
- Best wishes to Gina Charos who has accepted a position with Health Canada. ■

National Public Service Week 2005

The PMPRB dedicated June 15 to the National Public Service Week (NPSW) 2005. The day was set aside to recognize employees' achievements.

A *"WALK ON"* and a luncheon were organized to celebrate! ■

News from the Vice-Chairperson

2004 in review!

The Minister of Health tabled our Annual Report for 2004 before Parliament on June 14. Readers will have noted that we amended our Report this year, concentrating our efforts, among others, on the Reporting Information on Key Pharmaceutical Trends section. We re-organized this section in the hope that a more in-depth analysis of the key indices will assist our readers in better understanding the current context.

We reported that total sales of all drugs for human use by manufacturers in Canada increased 5.3% to $15.9 billion in 2004 from the previous year, while sales of patented drugs increased by 7.9% to $10.9 billion over

The Patented Medicine Prices Review Board is a quasi-judicial tribunal with the mandate to ensure that manufacturers' prices of patented medicines sold in Canada are not excessive.

Under the *Patent Act*, if the Chairperson is absent or incapacitated or if the office of Chairperson is vacant, the Vice-Chairperson has all the powers and functions of the Chairperson during the absence, incapacity or vacancy.

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Paul De Civita

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Ginette Tognet

Director of Corporate Services:
Robert Sauvé

Senior Counsel:
Martine Richard

You can contact us at:

Toll free-line:
1 877 861-2350

General number:
(613) 952-7360

Fax: (613) 952-7626

or e-mail us at:
pmprb@pmprb-cepmb.gc.ca

or write to us at:

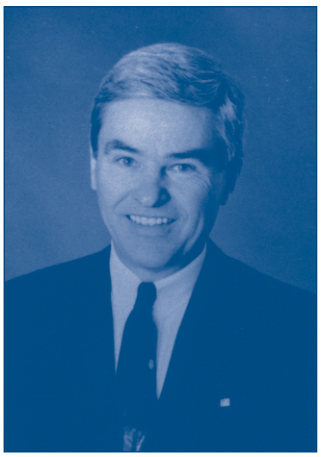
Box L40
Standard Life Centre
333 Laurier Avenue West
Suite 1400
Ottawa, Ontario
K1P 1C1

the same period. These annual rates of growth were the lowest recorded since 1997 and 1996 respectively. Patented drugs accounted for 68.6% of total drug sales, slightly higher than in 2003.

Prices of existing patented drugs fell by 0.2% from 2003. Analysis of prices by therapeutic class demonstrated considerable variability in price changes. The Canadian to foreign price comparison showed Canadian prices at 91% of the median of foreign prices in the seven countries used for price comparison purposes. With the exception of 2002, Canadian prices, on average, have been 5% to 12% below median foreign prices since 1995.

Ninety four new drug products came under the PMPRB's jurisdiction in 2004, including 25 new active substances. At the time of the release of this NEWSletter, 19 remained under investigation. Since January 2004 to date, enforcement activities resulted in ten Voluntary Compliance Undertakings (VCUs) by patentees ensuring that prices of patented medicines are within the Guidelines. The hearing into the price of the patented medicine Dovobet, initiated with the release of a Notice of Hearing in November 2004, is set to resume on September 12.

Patentees reported total R&D expenditures of $1.17 billion in 2004, a decrease of 2% over the $1.19 billion in 2003. The R&D-to-sales ratio continued its downward trend with the ratio for all patentees declining to 8.3% from 8.8% last year and Rx&D members' contribution declining to 8.5% from 9.1%. Spending on basic research increased by 23%, reaching $221.7 million, and representing 19.7% of current R&D.



Réal Sureau, Vice-Chairperson

We also reported on our latest initiatives with the public consultations on proposed amendments to the *Patented Medicines Regulations, 1994*, and on our Discussion Paper on Price Increases for Patented Drugs. Our review of both series of submissions received from stakeholders is ongoing, and next steps are scheduled for initial discussion at the September Board meeting. For additional information, see "2005 Consultations" on page 5 of this publication. Further developments on these initiatives will be published in our October NEWSletter.

It is our hope that our more in-depth analysis of key indices in our 2004 Report will foster a better understanding of the current pharmaceutical context as we strive to work in the best interest of all Canadians.

Before closing, I would like to take this opportunity to thank my colleagues on the Board and Staff. As I near the end of my second and final term as Vice-Chairperson of the Patented Medicine Prices Review Board in October, I want to thank everyone for their contribution to this organization. The PMPRB plays a significant role in protecting the interests of Canadians by ensuring that prices of patented medicines are not excessive. It has been both a pleasure and a privilege for me to serve as Vice-Chairperson of the PMPRB and I wish you all success in your endeavours and to the organization as a whole. ■

Réal Sureau
Vice-Chairperson

Questions and Comments

Please forward all subscriptions to the PMPRB e-mail or mailing lists and requests for publications to Elaine McGillivray at Elaine@pmprb-cepmb.gc.ca. For more information on our Web site, please contact our Communications Officer at pmprb@pmprb-cepmb.gc.ca. ■

Report on Pharmaceutical Expenditures (OECD)

In June 2005, the Organisation for Economic Co-operation and Development (OECD) released its annual update of health system statistics for developed countries. This year's edition provides statistics up to the year 2003, inclusively.

The following charts contain key OECD results for the pharmaceutical sector. This summary is limited to data for Canada and the seven countries the PMPRB considers in its international price comparisons[1].

Figure 1 shows pharmaceutical expenditure[2] as a share of total health care expenditure for the years 1990, 2000 and 2003. Pharmaceutical expenditure accounted for 16.9% of total health care expenditure in Canada in 2003, up from 15.2% in 2000 and 11.4 % in 1990.[3] Similar increases have occurred in France, Germany and the United States. In contrast, the share of pharmaceuticals has risen slightly or fallen in the remaining countries. Figure 1 shows the share of pharmaceutical expenditure in overall health spending ranges widely across countries, from 10.5 % in Switzerland to 22.1% in Italy. Canada's share, at 16.9%, puts it near the middle of this range.

Figure 2 gives pharmaceutical expenditure as a share of Gross Domestic Product (GDP). All countries spent a larger part of their GDP on drugs in 2003 than they had in 1990, and all have also seen increases relative to 2000. At the upper end, Italy, the U.S. and France reported ratios of 1.9%, 1.9% and 2.1%, respectively. Sweden, Switzerland and the U.K., on the other hand, all saw expenditure-to-GDP ratios of about 1.2%. Canada's ratio, at 1.7%, remains well within the range of values reported for the other countries and is only slightly less than the U.S. value. Critics of Canadian pharmaceutical policy regularly accuse this country of "free-riding" on research financed by consumers elsewhere. Based on Figure 2, its clear that Canada's spending on pharmaceuticals relative to its wealth is in line with other countries, and nearly equal to that of the U.S.

That Canada continues to pay its way is affirmed by Figure 3, which shows pharmaceutical expenditure per capita in U.S. dollars for 1990, 2000 and 2003.[4]

Figure 1
Pharmaceutical Expenditure as a Share of Total Health Care Expenditure

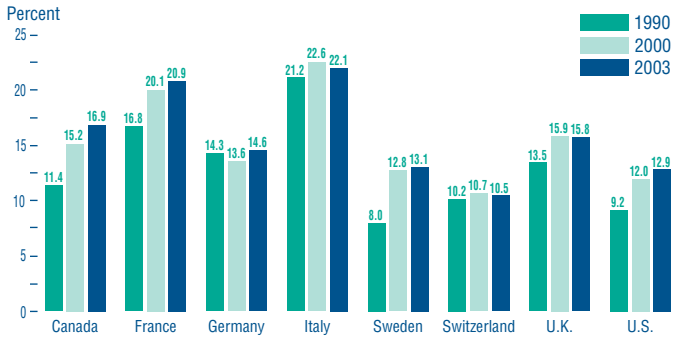
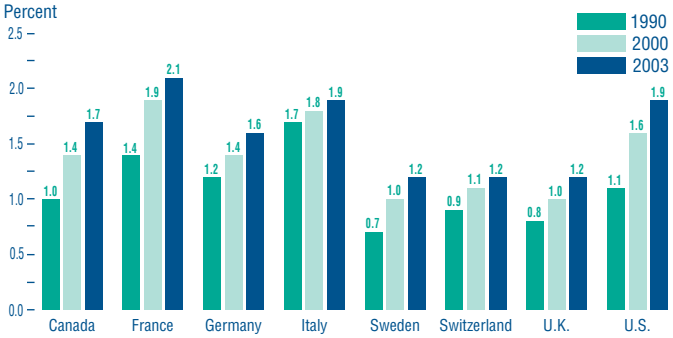


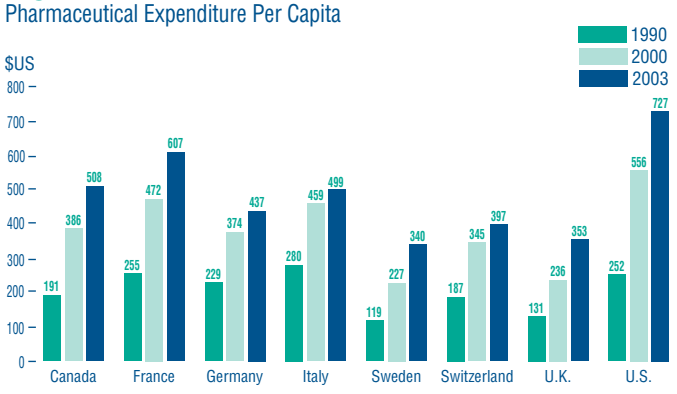
Figure 2
Pharmaceutical Expenditure as a Share of GDP



1. The comparator countries listed in the *Patented Medicines Regulations, 1994*, are France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States.
2. The OECD defines "pharmaceutical expenditure" as "total expenditure on pharmaceutical and other medical non-durables." This comprises "medical preparations, branded and generic medicines, drugs, patented medicines, serums, and vaccines, vitamins and minerals and oral contraceptives." It also includes non-pharmaceutical items such as toothpaste and condoms. The statistics reported encompass expenditure by both private and public sectors. Pharmaceutical expenditure may or may not include the value of drugs dispensed in hospitals, depending on the country.
3. In reporting results for Canada, the OECD uses estimates from the Canadian Institute for Health Information (CIHI) for both pharmaceutical expenditure and total health care expenditure. The share given for Canada in Figure 1 differs from that reported in other CIHI publications due to differences in the definition of total health care expenditure.
4. All expenditures reported here have been converted to U.S dollars at the OECD's Purchasing Power Parity exchange rates. This method of currency conversion implicitly corrects for international differences in the cost-of-living, which in turn permits international expenditure comparisons in terms of real cost (i.e., foregone consumption) rather than monetary units.

Only residents of France and the U.S. spent more per person on pharmaceuticals in 2003 than Canadians. Residents of all other countries paid less per person, considerably less in the cases of Sweden, Switzerland and the U.K. ■

Figure 3
Pharmaceutical Expenditure Per Capita



VCUs accepted during the last quarter

PMPRB

Ceretec (*technetium TC-99M exametazine*) is a radiopharmaceutical agent used for the diagnosis of brain diseases and tumors.

The full VCU is available on our Web site under "Publications"; "Voluntary Compliance Undertakings"; "Ceretec".

Starlix is indicated as monotherapy in addition to diet and exercise to lower the blood sugar in patients with type 2 diabetes mellitus who are not controlled satisfactorily by diet and exercise alone.

The full VCU is available on our Web site under "Publications"; "Voluntary Compliance Undertakings"; "Starlix".

Ceretec

On July 14, the Vice-Chairperson of the Board accepted the VCU for Ceretec, submitted by Amersham Health Inc.

The terms of the VCU require that, for purposes of the Guidelines, Amersham agree that the maximum non-excessive (MNE) price of Ceretec for 2004 was $173.1935 and is $177.7475 for 2005; ensure that the average transaction price (ATP) price of Ceretec does not exceed the MNE price of $177.7475 for 2005; and offset excess revenues of $278,112.65 it received from January 1, 2002 to December 31, 2004 by maintaining the price of Ceretec below the 2005 MNE price of $177.7475 until the end of December 31, 2005.

In the event any excess revenues have not been offset by the end of December 31, 2005, Amersham will make a payment to each of the customers (hospitals and institutions) that purchased Ceretec from January 1, 2002 to December 31, 2004. Each payment shall be calculated by taking the difference between the actual price paid and the MNE price at the time of purchase times the number of kits purchased over the period. All payments shall be made by January 31, 2006.

The price of Ceretec will remain under the PMPRB's jurisdiction until the expiry of the patent in April 2006.

Starlix

On July 25, the Vice-Chairperson approved a VCU submitted by Novartis Pharmaceuticals Canada Inc. for the patented medicine Starlix.

Under the terms of this VCU, Novartis undertook to reduce the price of Starlix 60 mg and 120 mg tablets so that the average transaction price in 2005 does not exceed the 2005 MNE price of $0.5044. Within 30 days of acceptance of this VCU, on or before August 25, 2005, Novartis will make a payment of $174,306.29 to the government of Canada for the excess revenues that accrued during the period March 2002 through June 2005.

Novartis will ensure that while patented, the average transaction prices of Starlix in Canada in future years does not exceed the maximum non-excessive prices calculated in accordance with the Guidelines. The price of Starlix will remain under the PMPRB's jurisdiction until the expiry of the patent in February 2014. ■

2005 Consultations

Earlier this year, the PMPRB launched two separate consultations with stakeholders to gain their input on different aspects of the PMPRB's work. In January 2005, a Notice and Comment was published proposing a number of amendments to the *Patented Medicines Regulations*, 1994, which set out patentees' filing requirements with respect to the PMPRB. In March 2005, a second Notice and Comment was issued asking for stakeholder input on how increases in patented medicine prices are reviewed. The PMPRB received a number of submissions from both consultations covering a variety of different viewpoints. Progress continues in the review of the stakeholder submissions and Staff is currently looking at next steps.

Proposed Amendments to the *Patented Medicines Regulations,* 1994

Developed as part of the PMPRB's Timelines Project to study and improve the timeliness and efficiency of the price review process, the purpose of the proposed amendments to the *Patented Medicines Regulations*, 1994 was to change when, how and what type of information patentees filed as part of the price review process.

Two proposals sought to require patentees to file a proposed price in advance of first sale and advance notice of a price increase. This would have allowed Board Staff to begin the review process earlier ensuring patentees had the relevant information on the status of their compliance with the PMPRB's Pricing Guidelines. While a number of stakeholders were in favour of such changes, patentees saw the change as problematic given the mechanisms of a competitive market. For those proposed amendments related to the type of information required of patentees, many stakeholders saw the changes as an effective tool for the PMPRB to gain a more complete insight into the pharmaceutical market and pricing. Patentees, on the other hand, were concerned about the potential impact of increased regulatory burden. There was also confusion over the mechanism of reporting. As for the remaining amendments, those dealing with the use of electronic signatures, increased precision on the filing requirements for veterinary drugs and editorial corrections, there was a general consensus in support of these changes.

Price Increases for Patented Medicines

In view of the reports of price increases in early 2004, the PMPRB launched a discussion paper to solicit stakeholder views on the issue of price increases for existing drugs. The discussion paper explained the current process and reviewed recent price trends. While the PMPRB made no specific proposals, respondents chose to focus primarily on two issues in their submissions: the establishment of a system of prior approval for price increases and changes to the factors used to gauge the appropriateness of price increases. Some submissions favoured a system of prior approval for price increases. Others questioned the need for such a major change given the lack of clear evidence of a problem. Some stakeholders recommended a more thorough use of all the existing factors outlined in the *Patent Act*. Still others advocated the review of price increases based new factors such as R&D expenditures or promotional spending of patentees.

In response to the two consultations, the PMPRB received a number of submissions that were both extensive and thoughtful, and we appreciate the efforts of those who responded. In the spirit of the PMPRB's commitment to transparency, all of the submissions received for both consultations are now posted on our Web site.

In terms of next steps, the Board will consider any changes to the proposed regulatory amendments at its next meeting in September. It will also discuss strategic options as to how to proceed on the matter of its approach in reviewing price increases. Additional information on both of these consultations will be communicated to stakeholders in subsequent issues of the PMPRB's NEWSletter. ■

This initial consultation is a first step in the federal regulatory process.

New Patented Medicines Reported to the PMPRB

As of June 30, 2005, there were 23 new DINs for human use (representing 14 medicines) reported to the PMPRB for the year 2005. Of these 23 DINs, 14 DINs (representing 7 medicines) are new active substances.

The following table presents the new active substances reported to the PMPRB during the period January to June 2005.

As of June 30, 2005

Brand Name	Generic Name	Company
Yasmin 21, Yasmin 28 (3/0.03)	drospirenone/ethinylestradiol	Berlex Canada Inc.
Strattera (10mg/cap; 18mg/cap; 25mg/cap; 40mg/cap;60mg/cap)	atomoxetine hydrochloride	Eli Lilly Canada Inc.
Telzir (700mg/tab; 50mg/ml)	fosamprenavir calcium	GlaxoSmithKline Inc.
Cipralex (10mg/tab; 20mg/tab)	escitalopram oxalate	Lundbeck Canada Inc.
Xolair (150mg/vial)	omalizumab	Novartis Pharma Canada Inc.
Zelnorm (6mg/tab)	tegaserod maleate	Novartis Pharma Canada Inc.
Nuvaring (0.12/0.015)	etonogestrel/ethinyl estradiol	Organon Canada Ltd. ■

Reports on New Patented Drugs – Humira

PMPRB

Under its transparency initiative, the PMPRB publishes the results of the reviews of new patented drugs by Board Staff, for purposes of applying the PMPRB's Price Guidelines for all new active substances introduced after January 1, 2002.

Brand Name: Humira

Generic Name: *(adalimumab)*

DIN: 02258595 40 mg syringe

Patentee: Abbott Laboratories Limited

Indication - as per product monograph: For reducing the signs and symptoms, and inhibiting the progression of structural damage in adult patients with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to one or more disease-modifying anti-rheumatic drugs (DMARDs).

Notice of Compliance: September 24, 2004

Date of First Sale: September 29, 2004

ATC Class: L04AA17
Antineoplastic and Immunomodulating Agents, Immunosuppressive Agents, Selective Immunosuppresive Agents

Application of the Guidelines

PMPRB

Summary Reports are available on our Web site under Patented Medicines; Reports on New Patented Drugs for Human Use.

Summary:

The introductory price of Humira was found to be within the Guidelines because the cost of therapy did not exceed the cost of therapy of existing drugs in the therapeutic class comparison and the price did not exceed the prices in the other comparator countries where Humira was sold.

Scientific Review:

Humira is a new active substance and the PMPRB's Human Drug Advisory Panel (HDAP) recommended that it be reviewed as a category 3 new medicine (provides moderate, little or no therapeutic advantage over comparable medicines).

The HDAP recommended Enbrel (*etanercept*), Remicade (*infliximab*) and Kineret (*anakinra*) as the most appropriate comparators for Humira. These products share the same fourth level ATC class, are all biological agents and are all indicated for the treatment of moderate to severe RA in patients who failed to respond to one or more synthetic disease modifying anti-rheumatic drugs.

As the treatment of RA is considered a chronic situation, the HDAP recommended that the maintenance dosage regimen of Enbrel, Remicade and Kineret be compared to the maintenance dosage regimen of Humira. Since the dosing frequency of the comparators varies so widely, the amount of respective drug that needs to be administered during one year was recommended for the purpose of establishing the Therapeutic Class Comparison (TCC).

Price Review:

Under the Guidelines, the introductory price of a new category 3 drug product will be presumed to be excessive if it exceeds the price of all of the comparable drug products in the TCC test, or if it exceeds the prices of the same medicine in the seven countries listed in the *Patented Medicines Regulations* (Regulations), that is France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States. The price of Humira was within the Guidelines as the daily cost of therapy did not exceed the cost of therapy with the comparator medicines.

Name	Dosage Regimen/per year	Cost Per Year
Humira (adalimumab)	40 mg every 2 weeks (26 syringes)	$20,186.66[1]
Enbrel (etanercept)	25 mg twice weekly (104 vials)	$17,160.00[2]
Remicade (infliximab)	5 mg/kg every 8 weeks (22.75 vials)	$21,385.00[2]
Kineret (anakinra)	100 mg daily (365 syringes)	$15,001.50[3]

1. PPS Pharma, January 2005
2. Régie de l'assurance maladie du Québec, February 2005
3. Le Guide du pharmacien propriétaire, Liste de l'AQPP, October 2004

In 2004, Humira was being sold in all of the seven countries listed in the Regulations. In compliance with the Guidelines, the price in Canada did not exceed the range of prices in those countries; the price of Humira in Canada was the lowest of those countries, below the median international price.

The Therapeutic Class Comparison (TCC) test of the Guidelines provides that the price of a category 3 new drug product cannot exceed the prices of other drugs that treat the same disease or condition. Comparators are generally selected from among existing drug products in the same 4th level of the Anatomical, Therapeutic, Chemical (ATC) System that are clinically equivalent in addressing the approved indication. See the PMPRB's *Compendium of Guidelines, Policies and Procedures* for a more complete description of the Guidelines and the policies on TCCs.

Evidence/ References:

The references are available on the PMPRB Web site, under Patented Medicines; Reports on New Patented Drugs for Human Use; Humira.

Where comparators and dosage regimens are referred to in the Summary Reports, they have been selected by the PMPRB Staff and the HDAP for the purpose of carrying out the PMPRB's regulatory mandate, which is to review the prices of patented medicines sold in Canada to ensure that such prices are not excessive. The publication of these reports is also part of the PMPRB's commitment to make its price review process more transparent.

The information contained in the PMPRB's Summary Reports should not be relied upon for any purpose other than its stated purpose and is not to be interpreted as an endorsement, recommendation or approval of any drug nor is it intended to be relied upon as a substitute for seeking appropriate advice from a qualified health care practitioner. ■

Patented Medicine Prices Review Board – May 17-18, 2005 Meeting

At this meeting, the Board:

- Approved the Annual Report for the year 2004 and the Communications Plan for its release;
- Was briefed on:
  - the National Pharmaceutical Strategy
  - the consultations initiated at the beginning of the year on the proposed amendments to the *Patented Medicines Regulations*, 1994, and on the Discussion Paper on Price Increases for Patented Medicines
  - the monthly compliance and investigation activities
  - the NPDUIS projects. ■

The next Board meeting is scheduled for September 23, 2005.

For additional information, please contact the Secretary of the Board at:

1 877 861-2350, or (613) 954-8299, or at sdupont@pmprb-cepmb.gc.ca.

Upcoming Events

August
16
HDAP Meeting, Ottawa

August 29 - September 2
29-2
International Conference on Pharmaceutical Drugs, Montréal

September
12-16
Dovobet Hearing, Ottawa

September
23
Board Meeting, Ottawa

October
18-19
Canadian Institute's Fourth Annual Forum on Pharma Patents, Toronto

October
20-21
The Canadian Institute's 5th Annual "Advanced Law and Practice" Conference – *Fundamentals of Administrative Law Practice*, Toronto

October
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October NEWSletter

November
17
HDAP Meeting, Ottawa

November
21-22
PHARMAC Sales & Marketing Summit 2005 – *"What does the future hold for drug price controls in Canada?"*, Toronto

November 29 - December 2
29-2
Dovobet Hearing, Ottawa

December
16
Board Meeting, Ottawa

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Comments

We want to hear from you. If you have any comments, ideas or suggestions on topics you wish to see covered in the NEWSletter, please let us know.

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Box L40
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Ottawa, Ontario
K1P 1C1

Fax: (613) 952-7626

E-mail:
pmprb@pmprb-cepmb.gc.ca

Toll-free number:
1 877 861-2350

Tel: (613) 952-7360

TTY: (613) 957-4373