Appendix: AstraZeneca Canada Inc. Technical Submission – March 2009 Draft Revised Excessive Price Guidelines

These are the technical submissions in support the comments found in the attached cover letter.

This submission is organized in accordance with the Patented Medicine Prices Review Board's (PMPRB's) Notice and Comment package on the Draft Revised Excessive Price Guidelines (Draft Guidelines) released on March 26, 2009. Other issues identified as a result of a review of the Draft Guidelines have also been included.

AstraZeneca urges the PMPRB to engage patentees in further information sessions and workshops to gain a better mutual understanding of the implications of the draft Guidelines prior to their full implementation.

Legal Framework

AstraZeneca Canada Inc. ("AstraZeneca") fully supports Canada's Research-Based Pharmaceutical Companies (Rx&D's) submission on this issue.

New terminology

AstraZeneca welcomes the proposed changes in terminology to address different uses of the term Maximum Non Excessive Price (MNE) in the current system, namely the introduction of the Maximum Average Potential Price ("MAPP") and the Non-Excessive Average Price ("NEAP"). However, AstraZeneca requestes that further clarity and guidance on how these new terms will be used in the daily operation of both the patentee's business and the PMPRB's function.

Introductory Price Tests

General Comments

AstraZeneca welcomes the introduction of a new category of therapeutic improvement that recognizes products that offer a moderate improvement over existing products. In addition, the PMPRB has addressed patentees' concerns regarding changes to the Reasonable Relationship Test (RRT) that would have resulted in disincentives to launch titration dosages for patentees. Both of these changes are a positive development for Canadian patients and patentees.

Therapeutic Class Comparison Test (TCC Test)

The use of the NEAP as the price benchmark for new product introductions in both the RRT and the TCC test raises significant concerns for AstraZeneca.

The PMPRB has recognized the importance of benefits offered by patentees to Canadian customers to improve access to new and innovative medicines; for example, as a result the PMPRB has introduced the DIP methodology in Schedule 10 of the Draft Guidelines. However, the proposed Draft Guidelines describe introductory price tests that reference a comparator product price that could be significantly decreased due to benefits offered by the patentee.

In addition, the introductory price of a new drug may reference a different comparator product price for the same product, depending on the time of launch of the new drug and benefits offered with the comparator product at that particular time. This is inconsistent, non-transparent and unpredictable.

The following example will illustrate the concern:

Therapeutic Class Comparison Test – Same Patentee introducing new Drug ABC - Top of the TCC is the price benchmark (referencing Drug XYZ).

Assumptions:
1. The introductory price in Year 1 for each class of customer is the public list price in Year 1, Year 2 and Year 3.
2. In Year 2, a $5.00 benefit is offered to Hospitals and a $2.00 benefit is offered to Wholesalers.
3. In Year 3, the Hospital and Wholesaler benefits are discontinued and their MS-NEAP* rebounds to the Year 1 price for the wholesaler and a blended price for the hospital as some other existing benefits continue.
4. The sales volume for each class of customer is 50% Hospital , 30% Wholesaler and 20% Pharmacy.

Drug XYZ	Hospital MS-NEAP*	Wholesaler MS-NEAP	Pharmacy MS-NEAP	National NEAP**
Year 1 (introduction)	$10.00	$9.00	$10.00	$8.70
Year 2 (benefit)	$5.00	$8.00	$10.00	$7.40
Year 3 (Dip Rebound PMPRB compliant)	$8.00	$9.00	$10.00	$8.70

* MS-NEAP refers to Market-Specific Non-Excessive Average Price
** National NEAP refers to National Non-Excessive Average Price

In Year 2, the patentee for Drug XYZ introduces a new Drug ABC in the same ATC class and for the same indication.

- Introductory price test = Therapeutic Class Comparison Test
- Comparator price = National-NEAP of Drug XYZ in Year 2
- Introductory Maximum Average Potential Price (MAPP) = **$7.40**

However, if the patentee were to delay the launch of the new drug until Year 3, the introductory MAPP would be the National-NEAP of Drug XYZ in Year 3, namely **$8.70**.

The PMPRB does not provide an explanation for recognizing a DIP at the end of a contract but not for the purposes of setting the MAPP of a new product. As a result, the patentees will be penalized for having their own benefit in place.

The determination of the MAPP is further complicated if the patentee of Drug ABC is referencing a product (Drug DEF) that is sold by a different company. Average transaction prices (ATP) or NEAPs are confidential and are known only to the patentee and the PMPRB. It is impossible for a patentee to predict the ATP/NEAP of another patentee's product accurately and with the level of certainty needed for to plan its own drug price. However, as the Guidelines are currently drafted, upon learning from the PMPRB what the MAPP for the new Drug ABC is when compared to Drug DEF, the patentee can determine, within a small range of prices, what the confidential NEAP for Drug DEF is.

The PMPRB has indicated that it will offer guidance to patentees in such circumstances, but it is questionable how the PMPRB can provide such guidance without potentially revealing confidential ATP/NEAP information. It is also unclear how the PMPRB can provide predictable, useful guidance to patentees given the business planning cycles industry operates under. Within global organizations, prices are considered many years before launch.

As such, AstraZeneca proposes that the PMPRB establish a different price benchmark for the introductory price test, one that does not rely on ATP/NEAP information.

There are several acceptable potential benchmarks for this purpose:

- The MAPP of a reference product at launch (or an adjusted MAPP should the National NEAP for this product exceeded the MAPP during the life of the brand), as published on the PMPRB website. The PMPRB could publish this price as part of the extended product review posted for category 2 and 3 products today; or
- A price published in a publicly available reference source such as a formulary; or
- The minimum price benchmark should be set the highest NEAP for a reference product, excluding all benefits, consistent with the DIP methodology

<u>International Therapeutic Class Comparison Test (ITCC Test)</u>

The main concern regarding the ITCC test as it is currently proposed is that generics are included. The ITCC should follow the same principle as the TCC and refer to the top of the ITCC as the price benchmark for any price comparison. AstraZeneca reiterates its view (which is supported by the recommendation of multi-stakeholder Working Group on International Therapeutic Class Comparison) that <u>all</u> generics should be excluded, unless the applicable price benchmark for the ITCC test is the top of the ITCC as proposed

because any generic comparison will significantly skew the results of the test. The PMPRB has not indicated why including some generics is necessary or beneficial.

Superior/Inferior product evaluation in new Category 4 price test

AstraZeneca agrees with the comments made by Rx&D in its submission.

Any Market Price Reviews

AstraZeneca agrees with the concerns and issues raised in the Rx&D submission.

The PMPRB has indicated in past discussions and consultations that an any market review after the benchmark period would only be necessary if an investigation was triggered. The Draft Guidelines are not aligned with this stated intention.

In addition, it is not clearly defined how a patentee would be informed by the PMPRB of any complaints filed with respect to the price of a product. This process should be more transparent and provide for a review of prices in the relevant market, but not necessarily trigger a full review in all markets.

The market reviews are further complicated by the possibility of the introduction and discontinuation of multiple benefits within a market sector.

For example, in any given year within the hospital market as defined by the PMPRB, it would be common to have an average of 5-8 contracts concluded, revised or renewed at various times during the year. Each contract could include single or multiple products. As a result, a product's price fluctuation may be strictly due to one of these contract changes during the course of the year. For example, in the case of a benefit discontinuation, the hospital may still purchase the product, but at the new price.

The complexity of the market place is far more difficult to assess than the examples provided by the PMPRB in discussions with patentees in information sessions to date.

AstraZeneca strongly recommends the PMPRB maintain its focus on the national average transaction price and expand its review into a relevant market only in exceptional circumstances.

Re-Setting the Non-Excessive Average Price after introduction

AstraZeneca encourages the PMPRB to revise its position on this point. Selling a product in Canada under the Special Access Program (SAP) prior to its full review and approval by Health Canada is not a common occurrence. Such sales are usually due to an unusually high level of unmet medical need in a specific area or the high potential promise a drug has shown in early clinical trials. These sales are limited, not for any commercial purpose and are only allowed after Health Canada has reviewed and approved each individual request.

AstraZeneca recommends that the PMPRB require that patentees make a full submission to the Board once a product previously sold under the SAP program receives its Notice of Compliance. At this time, the product can be assessed on its own merits, undergo a full review and assessment by the HDAP committee and obtain an introductory price in a similar way to any other new product introduction.

Neither the *Patent Act* nor the *Patented Medicines Regulations* prevent the PMPRB from adopting this simple and logical approach.

Recognizing Benefits (DIP Methodology)

AstraZeneca is fully supportive of the introduction of the DIP methodology by the PMPRB. However, it became apparent during the information session, the PMPRB has not sufficiently considered all the relevant applications of the DIP methodology, thus leaving patentees with a great deal of uncertainty in the areas of contract management, price tracking, price rebound and the application of the CPI methodology.

If, for example, a DIP existed in Year 1, but was eliminated in Year 2, the draft Guidelines would refer to an artificially reduced price in Year 1 as a key benchmark price if the patentee seeks to take an allowable price increase in Year 3. During the information sessions, the PMPRB acknowledged that this was an issue that would need to be addressed.

In addition, the PMPRB should clarify how it will approach the management of multiple DIPs within a market or how a DIP that could impact two markets will be applied (for example, a benefit to a buying group for hospitals operating only in a specific province).

Other Issues

Reporting requirements for patented products with generic competitors

AstraZeneca would suggest a further amendment to the Guidelines so that patented prescription drugs subject to generic competition are treated in the same fashion as OTC and veterinary products, namely their prices are reviewed only when a complaint is received.

Once a generic competitor enters the market, the price of the patented version of a drug not longer needs to be closely monitored given that there is set substitution of low cost alternatives in the provinces. Moreover, the underlying premise of regulating the prices of patented medicines is to ensure that patentees do not abuse their patent monopoly by charging excessive prices. Once generic competitors appear, the rationale for continued price regulation is highly questionable. This proposal would eliminate a significant level of administrative burden by reducing reporting requirements without removing the PMPRB's oversight of the prices of patented medicines.

Research & Development Reporting

The PMPRB reports annually on the innovative industry's R&D performance but this performance is currently only based on the definition of Scientific Research and Experimental Development (SR&ED in the *Income Tax Act*. Unfortunately, this definition excludes social sciences research, which includes such fields as health economics and epidemiological studies, both of which are increasingly being demanded from federal and provincial regulatory authorities in Canada.

In fact, as Canada's regulatory framework evolves, and patentees are required to generate even more scientific knowledge about the safety and effectiveness of medicines once they are on the market, efforts to provide the requested evidence will lead to increased investment in such research.

AstraZeneca believes that all research mandated by federal and provincial governments regarding patented medicines should be captured in the PMPRB's annual reporting to better recognize a patentee's true investment in R&D in Canada.