



Patented Medicine Prices Review Board

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# Compendium of Guidelines, Policies and Procedures

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## Note to the Reader

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# Compendium of Guidelines, Policies and Procedures

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The PMPRB first published the *Compendium of Guidelines, Policies and Procedures* in 1994 as a consolidation of its Guidelines, policies and procedures which had previously been published in various issues of its now defunct publication, the *Bulletin*.

From time to time since then, we have published clarifications of the Guidelines in the NEWSletter and consulted on amendments through our Notice and Comment process. Recently, we have updated the Compendium to incorporate amendments to the *Patented Medicines Regulations* as well as other revisions of a technical nature.

This updated version of the Compendium was first published on March 19, 2008.

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# Preamble

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The Patented Medicine Prices Review Board (PMPRB) is committed to making the price review process more open and transparent to all stakeholders.

Transparency plays a significant role in the area of pharmaceutical pricing – in terms of accessibility of information to all Canadians in order to assist them in the decision-making process regarding drug use. Increased transparency and openness in the PMPRB's process can contribute to fostering an environment that facilitates evidence-based decision-making for stakeholders, researchers, policy-makers and most importantly, the Canadian public.

In pursuit of the principle of transparency, the PMPRB will continue to respect the confidentiality of information. The PMPRB will also continue to promote voluntary compliance by the patentees.

## Introduction

This Compendium is a consolidation of the Guidelines, policies and procedures of the Patented Medicine Prices Review Board (PMPRB) previously published in Bulletins 1 through 19. It is divided into three chapters:

- Excessive Price Guidelines;
- Compliance and Enforcement Policy; and
- Scientific Review Procedures.

One of the PMPRB's primary objectives is to ensure that patentees are aware of the policies, procedures and Guidelines under which Board Staff review the prices of patented drug products, and proceed when a price appears to be excessive. This Compendium has been issued to promote awareness and facilitate compliance. Should there be any inconsistency, its contents supersede and replace all the directives previously published in Bulletins 1 through 19 inclusively.

## 1. Mandate

1.1 The mandate of the PMPRB is:

- to ensure that the prices of patented medicines charged by patentees are not excessive;
- to report annually to Parliament on its activities, and on pricing trends in the pharmaceutical industry; and
- to report annually on research and development (R&D) expenditures by the patented pharmaceutical industry and on the ratios of R&D expenditures to sales for individual patentees.

1.2 The PMPRB is responsible for reviewing the prices of all patented medicines sold in Canada for human or veterinary use, with the exception of those sold under a compulsory license granted by the Commissioner of Patents. Compulsory licenses granted on or after December 20, 1991 could not be exercised following amendments to the *Patent Act* (the Act) that came into force on February 15, 1993. New compulsory licenses ceased to be granted after February 15, 1993.

- 1.3 The PMPRB only reviews those prices charged by the patentee, usually to a wholesaler or directly to a hospital or pharmacy. Its jurisdiction does not extend to prices charged to consumers at the retail level.
- 1.4 Patent status is distinct from prescription status. Not all prescription medicines are patented; moreover, some non-prescription medicines sold over the counter are patented. In the context of the PMPRB mandate, the following definitions delineate its role, responsibilities and jurisdiction:

## **Medicine**

- 1.5 A medicine is defined as any substance or mixture of substances made by any means – whether produced biologically, chemically or otherwise – that is applied or administered in vivo in humans or in animals to aid in the diagnosis, treatment, mitigation or prevention of disease, symptoms, disorders, abnormal physical states, or modifying organic functions in humans or animals, however administered.
- 1.6 For greater certainty, this definition includes vaccines, topical preparations, anaesthetics and diagnostic products used in vivo, regardless of delivery mechanism (e.g., transdermally, capsule form, injectable, inhaler, etc.). This definition excludes medical devices, in vitro diagnostic products and disinfectants that are not used in vivo.

## **Patent**

- 1.7 For the purposes of its jurisdiction, the PMPRB considers as a patent any Canadian patent of invention that pertains to a medicine. This includes, but is not restricted or limited to, patents with the following status:
- patents for active ingredients;
  - patents for processes of manufacture;
  - patents for a particular delivery system or dosage form that are integral to the delivery of the medicine;
  - patents for indications; and
  - patents capable of being used, whether or not they are being worked.
- 1.8 With the exception of medicines sold under compulsory license, all patented medicines sold in Canada are covered by the PMPRB's price review jurisdiction, including:
- Patented single-source medicines;
  - Patented multi-source medicines, including those that are subject to competition from a generic copy made under a compulsory license;
  - Patented medicines sold as over-the-counter medicines or as prescription medicines;
  - Patented medicines sold under the Special Access Programme (SAP) or as Investigational New Drugs (IND).

## **Patentee**

- 1.9 The person for the time being entitled to the benefit of a patent pertaining to a medicine, including any other person entitled to exercise rights in relation to the patent, with the exception of a compulsory licensee.

## 2. The Board

- 2.1 The PMPRB was established pursuant to amendments to the [Patent Act](#) (the Act) that came into force on December 7, 1987. Further amendments, which came into force on February 15, 1993 enhanced the Board's powers, thereby encouraging patentees to price new and existing drugs in compliance with the PMPRB's Excessive Price Guidelines (Guidelines).
- 2.2 The Board is an independent and autonomous quasi-judicial body. To ensure this independence and autonomy, the Act provides no power, either expressly or implicitly, to the government to direct the Board or to review its decisions and orders. However, decisions of the Board are subject to judicial review by the Federal Court of Canada on jurisdictional or procedural grounds in accordance with administrative law principles.
- 2.3 As directed by the Chairperson, Board Staff carries out the day-to-day work of the PMPRB including the administration of the [Patented Medicines Regulations](#) (the *Regulations*), investigation of possible excessive price cases, ensuring compliance with the PMPRB's Guidelines, and the preparation for hearings.

## 3. Filing of Information

- 3.1 The PMPRB must have timely and accurate information on patented medicines to fulfill its mandate.
- 3.2 The Regulations require patentees to provide information pertaining to patented medicines for which a notice of compliance has been issued or that are being or have been sold in any market in Canada. The required information must be filed within the following time frames for so long as the reporting party remains a patentee:
  - [Section 82 of the Act](#) requires a patentee to notify the PMPRB of its intention to offer a drug product for sale and of the date on which sales are expected to begin, as soon as it is practicable to do so. However, information relating to the price need not be provided earlier than 60 days before the date on which the product is intended to be sold.
  - [Form 1](#) (Medicine Identification Sheet) within 7 days after the day on which the first Notice of Compliance is issued in respect of the medicine, or within 7 days after the day on which the medicine is first offered for sale in Canada, whichever comes first. Form 1 shall be accompanied by the product monograph for the medicine or, if a notice of compliance has not been issued in respect of the medicine, by information similar to that contained in a product monograph.
  - [Form 2](#) (Information on the Identity and Prices of the Medicine) within 30 days of the end of the following periods:
    - the day on which the medicine is first sold in Canada; and,
    - each first six-month period and last six-month period of every year, including the final partial period, during which the reporting party exercises rights under the patent.
  - [Form 3](#) (Revenues and Research and Development Expenditures) within sixty days after the end of each calendar year.

Reporting provisions for both patented veterinary and over-the-counter (OTC) drug products are outlined in Chapter 1, Section 10 of the Guidelines.



- 3.3 All required information referenced in section 3.2, provided to the Board by patentees, must be submitted using the appropriate electronic documents made available on the PMPRB Web site, under Regulatory. Patentees must send the completed electronic document, in its original format and file type, to the e-mail address specified on the Board's Web site.
- 3.4 The electronic documents provided by patentees must bear the electronic signature of an authorized individual, certifying that the information set out in the document is true and complete.
- 3.5 In addition, the Act endows the Board with specific powers to obtain, by order, other information it may require.

## 4. Protection of Confidential Information

- 4.1 Pursuant to [section 87 of the Act](#), apart from the exception noted below, any information or document provided to the PMPRB under section [80](#), [81](#) or [82](#) or in any proceeding under [section 83](#) is privileged, and cannot be disclosed without the authorization of the person who provided it, unless it has been disclosed at a public hearing under section 83.
- 4.2 Accordingly, the governing principle is that of confidentiality. However, there are exceptions. Under [subsection 87\(2\)](#), the above information may be disclosed to any person engaged in the administration of the Act under the direction of the Board; to the Minister of Industry or other Minister designated by the Regulations; and to the provincial ministers of health and their officials for the purpose of making representations to the Board with respect to a hearing under section 83.
- 4.3 Although section 87 of the Act aims to protect commercially-sensitive information, as well as some publicly available information i.e., ex-factory foreign prices, the privilege does not extend to information and materials collected by the PMPRB, including any analysis performed by the Board Staff of that information.
- 4.4 Information on the status of the price review by the PMPRB, including the compliance status of patentees and applicants, is not information supplied by patentees and therefore may be publicly available.
- 4.5 When the PMPRB has completed a review of a new patented medicine, and concluded that the price is within the Guidelines or does not warrant proceedings under the Act, and the patentee has been notified, information concerning the outcome of the price review may be made publicly available through the publishing of a summary report. The content of this report remains subject to the confidentiality provisions as outlined in paragraph 4.1 above.

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# Chapter 1 – Excessive Price Guidelines

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## 1. Purpose

- 1.1 [Subsection 85\(1\)](#) of the Act stipulates those factors that the Board, during the course of a public hearing, must take into consideration when determining whether a medicine is being sold or has been sold at an excessive price. These factors are:
- the prices at which the medicine has been sold in the relevant market;
  - the prices of other medicines in the same therapeutic class;
  - the prices of the medicine and of the other medicines in other countries;
  - changes in the Consumer Price Index; and
  - such other factors as may be specified by regulations.
- 1.2 If after considering the above factors, the Board is unable to determine if a price is excessive, it may consider the costs of making and marketing the medicine as well as other factors which can be specified by regulations or that the Board considers relevant in the circumstances.
- 1.3 The Board's *Excessive Price Guidelines* are issued pursuant to [section 96 of the Act](#). They are not a rigid set of decision-making rules and are not binding on the Board or on any patentee. They are intended to provide patentees with parameters and information that will aid them in establishing, in advance, prices that may be presumed not to be excessive.

## 2. Unit of Price Review

- 2.1 The PMPRB reviews the average price of each strength of an individual dosage form of each patented medicine. In most cases, the unit is consistent with the assigned Drug Identification Number, or DIN.
- Throughout these Guidelines, all units of review are referred to as a DIN or a drug product.
- 2.2 In cases when individual strengths of a dosage form are not assigned a DIN, the PMPRB will use each strength of an individual dosage form of such patented medicines as the basis of its price review. Such examples would include:
- Drugs available under the Special Access Programme
  - Investigational New Drugs
  - Medicines receiving a General Product (GP) number.
- 2.3 The price of a DIN will normally be expressed as the price per unit (also referred to as the average transaction price – see [section 5](#) at page 9 for further information) in which that DIN is sold (i.e., tablet, millilitre, inhaler, etc.) rounded to the fourth decimal place.

### 3. New vs. Existing Products

- 3.1 The Guidelines differentiate between "new" and "existing" drug products.
- 3.2 A new drug product is one for which the introductory price is under review. Drug products are considered new in the year during which they are introduced in Canada. New drug products are divided into three categories:

*Category 1* – A new DIN of an existing or comparable dosage form of an existing medicine.

*Category 2* – A new DIN of a non comparable dosage form of an existing medicine, or the first DIN of a new chemical entity that is a breakthrough or provides a substantial improvement over comparable existing DINs.

*Category 3* – A new DIN of a non comparable dosage form of an existing medicine, or the first DIN of a new chemical entity that provides moderate, little or no therapeutic advantage over comparable existing DINs.

For a complete description of the PMPRB's new drug product categorization process, please refer to the [Scientific Review Procedures](#) included in this Compendium.

- 3.3 Existing products are DINs for which a benchmark price has been established in accordance with the Board's Guidelines.

### 4. Investigational New Drugs and Special Access Programme

- 4.1 For drug products sold as Investigational New Drugs or under the Special Access Programme, the Board's Guidelines for new and existing drug products will be applied as appropriate.
- 4.2 The PMPRB recognizes that once a Notice of Compliance (NOC) has been obtained, it may be appropriate to adjust the benchmark price of a drug product first sold as an Investigational New Drug or under the Special Access Programme. In these cases, the average transaction price of the drug product following receipt of the NOC may be reviewed to determine if it appears to be excessive, based on the Guidelines applicable to new drug products.

### 5. Average Price and Net Revenue Calculations

- 5.1 The Regulations provide for the reporting of the average price per package or the net revenue from each package size of a DIN. Pursuant to the Regulations, the average price or the net revenue reported should take into account reductions given as a promotion or in the form of rebates, discounts, refunds, free goods, free services, gifts or any other benefit of a like nature after the deduction of the federal sales tax.
- 5.2 Adjustments made for free goods should only include products provided to customers in a saleable form, and in the same package sizes as those being offered for sale. Samples provided to physicians are not considered free goods, and patentees should not report them with the sales and price data submitted under the Regulations.

- 5.3 Products supplied under a compassionate release program can be either included or excluded from the calculation of the ATP, so long as the inclusion or exclusion thereof is consistent in all reporting periods.
- 5.4 For clarification see NEWSletter: Volume 4, Issue No. 2, April 2000, page 5 – [Calculation of the average transaction price in the event of special programs and incentives offered by patentees – clarification of the Board's Guidelines](#).
- 5.5 Generally, the average price will be calculated on the basis of the total net revenues for all package sizes of the DIN sold during the pricing period, divided by the number of units sold.

## 6. Excessive Price Tests

- 6.1 The PMPRB, in consultation with interested parties, has developed various tests to determine whether the price of a drug product is within the Guidelines.
- 6.2 The *Reasonable Relationship Test* considers the association between the strength and the price of the same medicine in the same or comparable dosage forms. The Reasonable Relationship Test is described in [Schedule 1](#).
- 6.3 The *Therapeutic Class Comparison Test* compares the price of the DIN under review with the prices of DINs that are clinically equivalent and are sold in the same markets at prices that the Board considers not to be excessive. This test is described in [Schedule 2](#).
- 6.4 The *International Price Comparison Test* compares the average transaction price of the DIN under review with the publicly available ex-factory prices of the same medicine sold in countries listed in the Regulations. This test is described in [Schedule 3](#).
- 6.5 The measurement of change in the Consumer Price Index (CPI) over a specified period is used to compare the average transaction price of a drug product with the CPI-adjusted price of the product. The calculation of the CPI-adjusted price is described in [Schedule 4](#).
- 6.6 The application of these tests in the PMPRB's review of the average price of a drug product is explained in the following sections.

## 7. All Patented Drug Products

- 7.1 The price of a new or existing patented drug product will be presumed to be excessive if it exceeds the prices of the same medicine sold in all countries listed in the Regulations. These prices will be determined using the International Price Comparison Test described in [Schedule 3](#).
- 7.2 As a transitional measure, when the price of a patented drug product in 1993 exceeded the prices in all other countries, the Board generally will not commence formal proceedings if it is satisfied that appropriate action is being taken to ensure that the price will comply with the Guidelines by January 1, 1996. Specifically, the prices of such drug products must not increase in 1994. When a price freeze in 1994 and 1995 is insufficient to achieve compliance with the Guidelines, the patentee will be required to reduce prices in 1995 and, if necessary, in 1996. In the absence of evidence that a patentee or former patentee has taken appropriate action, the Board may commence formal proceedings based on prices prevailing after January 1, 1994.
- 7.3 The application of this Guideline is in addition to the PMPRB's Guidelines for new and existing drug products described in the following sections.

## 8. New Drug Products

8.1 The test applicable to the introductory price of a new DIN is dependent upon the category recommended for the drug product during the scientific review process.

### 8.2 Benchmark Period

The introductory price of a new drug product is determined by calculating the average transaction price (ATP) of the DIN during the benchmark period, i.e., from the date of first sale to the end of the six-month regulatory reporting period (June 30 or December 31), as long as the period covered is greater than one month. If the period is less than one month, the following six-month reporting period will be used.

### 8.3 Category 1 New Drug Products

In addition to the Guideline applicable to all patented drug products detailed in Section 7, the introductory price of a Category 1 new drug product will be presumed to be excessive if it does not bear a reasonable relationship to the average price of other DINs of the same medicine in the same or comparable dosage forms ([Schedule 1](#)).

When the above methodology is not considered adequate or appropriate, Board Staff may conduct a Therapeutic Class Comparison Test ([Schedule 2](#)) to determine if the introductory price of the new DIN is excessive. This could be relevant if, for example, the new DIN has a therapeutic use or dosage regimen that differs materially from the other DINs of the same or comparable dosage forms of the medicine.

While the introductory price of a Category 1 DIN will normally be compared against DINs of the same patentee, Board Staff may consider it appropriate in some instances to include DINs of other patentees. (For example, another voluntary licensee of the same patent as that pertaining to the new drug product, or a patentee marketing a drug product containing the same active ingredient as the new drug product but for which a different patent pertains.)

## Modified Release Formulations

Drug products with modified release formulations are ordinarily considered Category 1 new drug products (line extensions), and are therefore subject to the Reasonable Relationship Test. However, the Reasonable Relationship Test may not be appropriate when the use of a modified release formulation provides a lower price per treatment to the consumer than the conventional release formulation.

Specifically, where a patentee can demonstrate that the price per treatment of a modified release formulation is less than the price per treatment of the conventional release formulation of the same or comparable dosage form of the same medicine, Board Staff may consider such information as evidence that the Reasonable Relationship Test is not adequate or appropriate.

Under such circumstances, a Therapeutic Class Comparison Test will be conducted but ordinarily it will be restricted to comparing the modified release presentation to the conventional release presentations of the same or comparable dosage form of the same medicine from the same patentee.

### 8.4 Category 2 New Drug Products

The introductory price of a Category 2 new drug product will be presumed to be excessive if it exceeds the prices of all comparable drug products, based on a Therapeutic Class Comparison Test ([Schedule 2](#)), and the median of the international prices identified in an International Price Comparison Test ([Schedule 3](#)).

In addition, the Guideline applicable to all patented drug products detailed in Section 7 will apply in cases when the introductory price of the new DIN exceeds the median international price but does not exceed the prices of all comparable drug products, based on a Therapeutic Class Comparison Test.

#### 8.5 **Category 3 New Drug Products**

In addition to the Guideline applicable to all patented drug products detailed in Section 7, the introductory price of a Category 3 new drug product will be presumed to be excessive if it exceeds the prices of all of the comparable drug products based on a Therapeutic Class Comparison Test ([Schedule 2](#)).

8.6 When it is inappropriate or impossible to conduct a Therapeutic Class Comparison Test, Board Staff will give primary weight to the median of the international prices identified in an International Price Comparison Test ([Schedule 3](#)) to determine if the introductory price of the new DIN is excessive.

8.7 Unless the introductory price of the new DIN is outside the Guidelines, it will establish the benchmark price. If the introductory price exceeds the Guidelines, the maximum non-excessive price will establish the benchmark price. Thereafter, the price will be reviewed using the test applicable to existing DINs.

## 9. Existing Drug Products

9.1 In addition to the Guideline applicable to all patented drug products detailed in Section 7, the price of an existing DIN will be presumed to be excessive if it exceeds the benchmark price of the DIN adjusted for the cumulative change in the Consumer Price Index (CPI) from the benchmark period to the pricing period under review (CPI-adjusted price). [Schedule 4](#) provides detailed definitions and examples of the PMPRB's CPI-adjustment methodology.

9.2 Regardless of the above, and in addition to the Guideline applicable to all patented drug products detailed in Section 7, one-year price increases in the current pricing period may not exceed 1.5 times the forecast change in the annual CPI. In periods of high inflation (over 10%), the limit will be five percentage points more than the forecast change in the CPI.

9.3 The Board recognizes that the actual change in the CPI may be less than forecast. Where the patentee uses the forecast CPI, as described in [Schedule 4](#), a price discrepancy that arises solely from the use of the methodology will not automatically trigger a price review.

9.4 This CPI-adjustment methodology came into effect on January 1, 1994. As a transitional measure, a patentee with a product whose price in 1994 and 1995 faces a reduction solely as a result of the change in the CPI-adjusted methodology is not required to lower the price from the non-excessive average price of the previous year. A price at the same level as the previous year will be considered to be within the Guidelines.

#### 9.5 **Existing Drug Products Subsequently Sold by Another Patentee**

Where an existing drug product is sold in Canada by persons other than the initial patentee, the PMPRB's Guidelines will apply to the DINs sold by these persons as if they were the DINs of the initial patentee. For example, if a patentee ceases to sell a patented drug product and the marketing rights to the product are transferred to another patentee, the new DIN will be considered as a continuation of the original DIN for purposes of the application of the Guidelines.

## 10. Provisions for New and Existing Veterinary and Over-the-Counter (OTC) Drug Products

- 10.1 The following provisions (10.2 - 10.8) apply to all new and existing drug products, where the medicine is for human use and does not contain a controlled substance as defined in the *Controlled Drugs and Substances Act* or does not contain a substance listed or described in Schedule C or D to the *Food and Drugs Act* or in Schedule F to the *Food and Drug Regulations* or is a medicine for veterinary use (henceforth referred to as veterinary and OTC medicines).
- 10.2 All veterinary and OTC patentees are required to continue to notify the PMPRB, in accordance with [section 82 of the Act](#), of their intention to offer a medicine for sale and of the date on which sales are expected to begin, as soon as it is practicable to do so.
- 10.3 All veterinary and OTC patentees are required to continue to report information identifying the medicine, using [Form 1](#), no later than the earlier of seven days after the day on which the first Notice of Compliance is issued in respect of the medicine, and the medicine is first offered for sale in Canada, whichever comes first.
- 10.4 Subsequent to a change in the [Patented Medicines Regulations](#), patentees of new and existing veterinary and OTC medicines are no longer required to provide information respecting the identity and price of a medicine ([Form 2](#)) for the day on which the medicine is first sold, nor for each six-month period beginning on January 1 and July 1 of each year. Patentees must retain that information in the event it becomes necessary.
- 10.5 Upon receiving a substantiated complaint, Board Staff will conduct an investigation of the price at which a manufacturer is selling that patented veterinary or OTC medicine. A substantiated complaint is one which is accompanied by evidence, oral or written, which provides grounds to believe that a price may not be in compliance with the Act.
- 10.6 In the event of an investigation, the veterinary or OTC patentee shall within 30 days of a request from the Board, file information on the identity and price of the medicine ([Form 2](#)) for the relevant time period specified in the request. In addition, patentees will also be required to file information on the identity and price of the medicine for two years following the request, within 30 days after each six-month reporting period.
- 10.7 If Board Staff concludes that the price is not in compliance with the Act, the matter will be referred to the Chairperson in accordance with the [Compliance and Enforcement Policy](#). Under the policy, a patentee will be given opportunities to provide additional information and to submit a written proposal in the form of a Voluntary Compliance Undertaking to adjust its price.
- 10.8 Where, following an investigation, a price is found to be in compliance with the Act, a report to the Chairperson will be prepared for closure. To ensure transparency, the resolution of all investigations which follow from a complaint received by the PMPRB, for both new and existing patented veterinary and OTC medicines, will be made publicly available.
- 10.9 The provisions for veterinary and OTC patentees do not affect the jurisdiction and powers of the Board under the Act nor do they fetter in any way the Board's discretion in carrying out its duties and responsibilities under the legislation.

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## **Chapter 2 – Compliance and Enforcement Policy**

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### **1. Purpose**

- 1.1 The purpose of this policy is to ensure that the prices of patented medicines are not excessive by encouraging and facilitating voluntary compliance by pharmaceutical patentees with the Act.
- 1.2 The policy is based on the following principles:
  - a) Consultation with all interested parties, including patentees and ministers of health, on the development of Regulations, Guidelines and other policies of the Board.
  - b) Clear Regulations and Guidelines to provide certainty concerning the filing requirements and price review criteria.
  - c) Transparency of the PMPRB's policies and activities to the extent consistent with the provisions of the Act.
  - d) Fair proceedings in accordance with the principles of natural justice.
  - e) Timely and effective enforcement to remedy instances of excessive pricing, deter non-compliance with the Act, and penalize, when appropriate, activities contrary to the Act.

### **2. Information and Consultation**

- 2.1 The PMPRB's Regulations, Guidelines and Policies shall be developed in an open manner with opportunities for full consultation with interested parties.
- 2.2 The Guidelines shall be published and made available to all interested parties; the PMPRB will make every reasonable effort to assist patentees to understand the Guidelines and their application.
- 2.3 To the extent consistent with the Act and the overall objectives of this Policy, the PMPRB will report publicly on its activities on a regular basis.

### **3. Advisory Assistance and Non-binding Certificates**

- 3.1 The Guidelines are intended to provide clear criteria to permit patentees to set prices that will not be presumed to be excessive. Board Staff will also assist patentees, in the ways set out below, to determine if a proposed price would conform to the Guidelines.
- 3.2 Board Staff will advise a patentee on the appropriate methodologies to be applied to review the price of a new drug product.
- 3.3 At the request of a patentee, and if sufficient information is available, Board Staff will ask the Human Drug Advisory Panel (HDAP) to recommend the category of a new drug product before it is first sold.



- 3.4 At the request of a patentee, and if sufficient information is available, Board Staff will provide a non-binding opinion as to whether a proposed price would be within the Guidelines.
- 3.5 At the request of a patentee, and if sufficient information is available, the Board may, if it is satisfied that the price at which the patentee is selling or proposes to sell a patented drug product would not be found to be excessive, issue a non-binding certificate to that effect under [subsection 98\(4\)](#) of the Act.

## 4. Categorization of New Drug Products

- 4.1 The Human Drug Advisory Panel (HDAP) will recommend the category for all new active substances. For all other new medicines, Board Staff will recommend the category. Where there is some doubt on the part of Board Staff, the matter will be referred to the HDAP.
- 4.2 Only the Panel, and not Board Staff, may recommend that a new medicine be considered a breakthrough or substantial improvement (Category 2).
- 4.3 The PMPRB will publish summary reports on the results of the price review for all new active substances, including all drugs considered to be breakthroughs or substantial improvements. The PMPRB may publish the results of other reviews as is determined appropriate.
- 4.4 If a patentee wishes the PMPRB to consider evidence supporting scientific claims, it should submit that evidence in advance of Board Staff's review of the introductory price (i.e., prior to the date when price data must be filed for the first day of sales).
- 4.5 Additional evidence submitted by a patentee subsequent to Board Staff's review of the introductory price will be reviewed by the HDAP, but such review shall not delay the compliance and enforcement process.
- 4.6 At the request of the patentee, and where sufficient information is available, Board Staff or the HDAP will recommend a category before the drug product is first sold.

## 5. Review of the Prices of Patented Medicines

- 5.1 Board Staff review the prices of all patented medicines on a regular basis to ensure they conform to the Guidelines. The reviews are based on the filings by patentees pursuant to the Regulations, but may include information from other sources such as complainants.
- 5.2 Where a price appears to be outside the Guidelines, Board Staff may conduct an investigation. Criteria for commencing an investigation are identified in [Schedule 5](#).
- 5.3 These criteria are subject to change. They represent the standards the Board applies in order to allocate its resources to investigations as efficiently as possible. Their existence should not be construed as indicating that the Board accepts any deviation from the Guidelines. The Board is satisfied that its criteria assure that all significant cases of pricing outside the Guidelines will be subject to investigation.
- 5.4 The Board expects the prices of all patented medicines to be within the Guidelines and evidence of persistent pricing outside the Guidelines, even by a small amount, may be used as a criterion for commencing an investigation.

## 6. Investigations

- 6.1 When it finds that the price of a patented drug product appears to exceed the Guidelines, and the circumstances are within the criteria established by the Board from time to time, Board Staff will conduct an investigation to determine the facts.
- 6.2 Board Staff will advise the patentee immediately that it has commenced an investigation.
- 6.3 The investigation will include an analysis of the pricing history of the drug product and may include an investigation of the prices being paid for the drug product by customers, including public and private drug plans and hospitals.
- 6.4 The period of time available to the patentee to respond to Board Staff is ordinarily brief. For example, if the patentee should have known that a price was outside the Guidelines based on its own filings (e.g., CPI-adjusted price), the period of time may be as short as seven calendar days. A longer period of time, perhaps 30 calendar days, may be available if it is reasonable to believe that the patentee might have been unaware that there would be a problem (e.g., if the HDAP has recommended use of different comparators or dosage regimens from those which may have been reasonably anticipated by the patentee).
- 6.5 If the investigation reveals that the price of the drug product was not outside the Guidelines, Board Staff will terminate its investigation and advise the patentee accordingly.
- 6.6 If the investigation confirms that the price exceeded the Guidelines, the matter will be referred to the Chairperson of the Board. The patentee will be given an opportunity to submit a written proposal in the form of a Voluntary Compliance Undertaking (VCU) to adjust its price and will be advised that a report on the investigation will be forwarded to the Chairperson.
- 6.7 The patentee can submit a VCU at any time during the course of an investigation. Board Staff, however, is not authorized to terminate an investigation in the event of a proposed VCU. Rather, the undertaking will be communicated along with Board Staff's report on the investigation to the Chairperson.
- 6.8 If the Chairperson concludes that additional information is required concerning the price at which the drug product is being sold or has been sold in any market in Canada or elsewhere, the Chairperson may, on behalf of the Board, pursuant to [subsection 81\(1\) of the Act](#), make an order or orders requiring the production of such information.
- 6.9 If a patentee has provided a notice of intended sale of a drug product under [subsection 82\(1\) \(Schedule 6\)](#), or if the Chairperson has reason to believe that a patentee intends to sell a drug product in a market where it has not been previously sold, he may, on behalf of the Board, pursuant to [subsection 82\(2\)](#), make an order or orders requiring the production of information or documents respecting the proposed introductory price.

## 7. Voluntary Compliance Undertakings (VCUs)

- 7.1 A patentee may make a VCU to adjust its price and to take other remedial action as may be appropriate at any time.
- 7.2 It is the policy of the Board that only the Chairperson or the Board itself may approve a VCU.
- 7.3 The Chairperson is authorized to approve a VCU in lieu of issuing a Notice of Hearing if satisfied that it meets the objectives of the Act and conforms to the policies of the Board which may be established from time to time. If the undertaking is made after the issuance of a Notice of Hearing, it may only be approved by the Hearing Panel of the Board as a basis for terminating or adjourning the proceeding following an opportunity for submissions by all parties.
- 7.4 The Chairperson is not authorized to negotiate the terms of a VCU with a patentee. In deciding whether to accept a VCU, the Chairperson will be guided by [section 83 of the Act](#) and the policy of the Board that the price should be adjusted to conform to the Guidelines and that the patentee offset any excess revenues received since the price first exceeded the Guidelines.
- 7.5 The proposed VCU should include a statement as to the maximum price the patentee proposes to charge for the drug product, and the relevant dates, to be consistent with the Guidelines and policies of the Board, and where appropriate, the means by which it proposes to, offset the excess revenues it received during the period the price was outside the Guidelines.
- 7.6 In most cases, the VCU should specify a payment to Her Majesty in Right of Canada as the means to offset excess revenues.
- 7.7 The proposal of a VCU does not constitute an admission by the patentee that the price of the drug product is or was excessive.
- 7.8 The Board will report publicly on all VCUs accepted by the Chairperson or the Board. The information reported will ordinarily include the names of the drug product and the patentee and such other information as it considers appropriate. This information will be included in the PMPRB's Annual Report and may also be published in the NEWSletter, on the PMPRB Web site or other publications. Privileged or confidential information will not be included in the report except to the extent that such information has been made public in a proceeding.

## 8. Remedial Orders

- 8.1 If the Chairperson is of the view that the investigation has revealed that the price exceeded the Guidelines or otherwise may be or has been excessive, the Chairperson may commence a formal proceeding by issuing a Notice of Hearing and establishing a Hearing Panel of the Board for that proceeding.
- 8.2 The determination by the Board of the appropriate remedy, if any, in any case will be made by the Board in light of the evidence available to it.
- 8.3 Where the Board finds, following a public hearing, that the price of a patented drug product is excessive, it may make an order pursuant to [subsection 83\(1\)](#) requiring the patentee to reduce the price of the drug product to a level the Board considers not to be excessive.

- 8.4 In addition, the Board may order the price to be further reduced, pursuant to [subsection 83\(2\)](#), for a specified period of time to offset any excess revenues received by the patentee. The Board will take into consideration any submissions as to why it may be inappropriate to order such a reduction given the facts of the case.
- 8.5 In the alternative, or in addition to a price reduction order, the Board may order a price reduction with respect to one other patented medicine being sold by the patentee.
- 8.6 In the case of a former patentee, the Board may order, pursuant to [subsection 83\(3\)](#), a reduction in the price of another patented medicine to offset the excess revenues received by the former patentee.
- 8.7 If the above remedies are not considered appropriate, or if there are no medicines with respect to which the Board may make an order, the Board may order the payment by the patentee to Her Majesty in Right of Canada under [subsection 83\(2\)](#), or by the former patentee, under [subsection 83\(3\)](#), as the case may be, of an amount equal to the excess revenues.
- 8.8 If the Board finds that there has been a policy of selling the drug product at an excessive price, for example if the patentee has failed to comply with a previous price reduction order, the Board may, pursuant to [subsection 83\(4\)](#), order further price reductions or monetary payments to recover twice the excess revenues received by the patentee.
- 8.9 All orders by the Board, under [section 83](#), will be registered with the Federal Court of Canada pursuant to [section 99](#), and may be enforced thereafter, in the discretion of the Board, as an order of the Federal Court.
- 8.10 Evidence that a patentee has failed to comply with an order of the Board under [section 83](#) respecting price will be brought to the attention of the Chairperson who may decide to issue a Notice of Hearing.
- 8.11 If the Board finds that a patentee has failed to comply with an order of the Board respecting price under [section 83](#) it may issue a further order including an order to recover double the excess revenues if it finds that there has been a policy of selling at an excessive price.
- 8.12 At any time, in lieu of or in addition to the Board's own proceeding, the Board will refer any evidence that the patentee intentionally failed to comply with an order respecting price to the Attorney-General of Canada for proceedings under [subsection 76\(1\)](#) or contempt of court as may be appropriate.

## **9. Sanctions for Failure to File or to Comply with an Order to Produce Documents**

- 9.1 Evidence of failure to file a Notice of Intended Sale, pursuant to [subsection 82\(1\)](#) or information that is required under the Regulations, will be brought to the attention of the Chairperson who may issue an order requiring production of information.
- 9.2 Pursuant to [subsection 82\(2\)](#) the Board may require a patentee to provide information and documents respecting the price at which a drug product is intended to be sold. [Schedule 6](#) identifies the filing requirements for the notification of intent to sell.

- 9.3 If it appears to the Chairperson or to the Board that the patentee failed to file with the Board to escape or delay the review by the Board of the price of a patented medicine, the Board may also refer the matter to the Attorney-General of Canada to determine if proceedings should be commenced under [subsection 76\(1\)](#).
- 9.4 Orders by the Board under section [80](#), [81](#), [82](#) or [88](#) may be registered with the Federal Court of Canada pursuant to [section 99](#).
- 9.5 Evidence of failure to comply with a Board Order made under section [80](#), [81](#), [82](#) or [88](#) will be referred to the Attorney-General of Canada for proceedings under [subsection 76\(1\)](#) or for contempt of court, as appropriate.
- 9.6 Instances of failure to file some portion of the information regarding current sales of a patented medicine and research and development expenditures in accordance with the Regulations will be examined by Board Staff. In those cases that do not prevent Board Staff from reviewing the price of a drug product, the patentee will be given a reasonable period of time to file the missing information. Other cases may be referred to the Chairperson for disposition, including the issuance of an order by the Board to produce information.

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## Chapter 3 – Scientific Review Procedures

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### 1. Purpose and Approach

- 1.1 This chapter presents the principles and procedures followed by the PMPRB when categorizing new drug products and selecting comparable medicines, dosage forms and dosage regimens.
- 1.2 The PMPRB considers it desirable to seek the advice of experts such as advisory panel. The advisory panel and Board Staff prepare recommendations for the determination of categories for new drug products.
- 1.3 Recommendations are based on information provided by the patentee, publicly available scientific literature, and the expertise of each member of the advisory panel and Board Staff.
- 1.4 The Board cannot delegate its statutory obligations nor fetter its discretion; hence recommendations provided by the panel and Board Staff cannot be and are not binding on the Board.

### 2. Human Drug Advisory Panel (HDAP)

- 2.1 The HDAP meet as required.
- 2.2 The Board established the HDAP to provide recommendations for the categorization of new drug products and the selection of comparable drug products.
- 2.3 The HDAP perform the following functions:
  - review and evaluate scientific information available to the PMPRB (including submissions by patentees);
  - consider advice from other experts (when deemed necessary); and determine, by majority vote, a recommendation of the category of the new drug product, comparable drug products and dosage regimens.
- 2.4 The panel may call on other experts as required for additional advice. These outside experts are not members of the panel and do not vote.
- 2.5 Members of the panel and other scientific experts called upon to give advice are provided with the PMPRB's criteria to be used in their recommendation of category for new drug products.
- 2.6 The panel do not mediate or resolve disputes over a drug product's category, and they do not meet with patentees.
- 2.7 The names of the members of the panel are available to patentees upon request.

### 3. Categories

- 3.1 A Category 1 drug product is a new DIN of an existing dosage form of an existing medicine, or a new DIN of another dosage form of the medicine that is comparable to the existing dosage form as per [Schedule 7](#).
- 3.2 A Category 2 drug product is one that provides a breakthrough or substantial improvement. It is a new DIN of a non-comparable dosage form of an existing medicine or the first DIN of a new chemical entity.
- 3.3 A Category 3 drug product is a new DIN of a non-comparable dosage form of an existing medicine or the first DIN of a new chemical entity. These DINs provide moderate, little or no therapeutic advantage over comparable medicines. This group includes those new drug products that are not included in Category 2 above.

### 4. Primary Indication

- 4.1 Indication is not considered in the categorization of drug products that are new DINs of a comparable dosage form of an existing medicine (Category 1).
- 4.2 Determining the primary approved indication is important for the categorization of a new drug product with multiple approved indications that is either the first DIN of a new chemical entity, or the first DIN of a non-comparable dosage form of an existing medicine (Category 2 and Category 3 drug products). Determining primary approved indication is also important for the selection of comparable medicines.
- 4.3 New DINs with multiple approved indications (that are new chemical entities or new, non-comparable dosage forms of existing chemical entities) will be categorized based on the approved indication for which the medicine offers the greatest therapeutic advantage in relation to alternative therapies for the same indication in a significant patient population. This would exclude rare medical conditions or diseases (i.e., low incidence and prevalence in Canada).

This approved indication will be considered the "primary use" indication for the purposes of selecting comparable medicines.

- 4.4 Where there is no apparent single approved indication for which the medicine offers the greatest therapeutic advantage (e.g., the drug is a breakthrough for two indications), the approved indication representing, potentially, the greatest proportion of sales will be the basis for categorization and selection of comparable medicines.

Estimates of potential sales can be based on several sources including actual prescribing patterns (when available), epidemiological data (Canadian incidence and prevalence) and prescribing patterns in other countries.

## 5. Defining Breakthroughs or Substantial Improvements

- 5.1 A breakthrough drug product is the first one to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication.
- 5.2 A drug product constituting a substantial improvement is one that, relative to other drug products sold in Canada, provides substantial improvement in therapeutic effects (such as increased efficacy or major reductions in dangerous adverse reactions) or provides significant savings to the Canadian health care system.
- 5.3 While the determination of breakthrough medicines should be relatively straightforward, difficulties can occur in the identification of medicines that offer substantial improvement (Category 2) rather than moderate improvement (Category 3), primarily in borderline cases.
- 5.4 To determine if a new drug product provides a substantial therapeutic improvement over previously available medicines, the PMPRB will review evidence in support of either increased efficacy or major reductions in dangerous adverse reactions for the new DIN over other available medicines.

In both these cases, the performance of the new drug product will be reviewed taking into consideration its clinical indications, as listed in the product monograph. The affected population to be considered will be the one targeted by the approved indication(s).

- 5.5 The PMPRB may also take other factors into consideration when determining whether a new drug product provides a substantial improvement. These may include:
- time required to achieve the optimal therapeutic effect;
  - length of treatment;
  - percentage of affected population treated effectively;
  - success rate; or
  - the route of administration when leading to a reduction in adverse effects.

Each factor will be weighted with respect to its clinical significance in therapy for the particular therapeutic class.

- 5.6 In categorizing new drug products, factors such as the following will not generally be taken into consideration:
- the mechanism of action;
  - a new chemical entity;
  - improved compliance;
  - greater patient convenience;
  - the therapeutic index; or
  - a different pharmacokinetic profile

unless the result is either increased efficacy or a major reduction in dangerous adverse reactions.



## 6. Submissions for All Categories

- 6.1 For each new drug product (DIN) they propose to market, patentees are required to provide Board Staff with the product monograph for the medicine, or if a Notice of Compliance has not been issued in respect of the medicine, with information similar to that contained in a product monograph.
- 6.2 Patentees are also requested to provide Board Staff with a brief submission which includes the following information:
  - a. the proposed category for the new DIN (refer to [section 3](#));
  - b. the proposed primary use of the drug product for new DINs with multiple approved indications (refer to [section 4](#));
  - c. the proposed comparator drug product(s) for the price review of the new DIN (refer to [section 8, page 11, Excessive Price Chapter](#); and [section 9](#));
  - d. the proposed comparable dosage regimens for the new DIN and each of the comparator drug products identified in c);
  - e. where it is reasonable to expect that a therapeutic class comparison will be conducted (refer to section 8, page 11, [Excessive Price Chapter](#); and [section 10](#)).
- 6.3 Each submission should clearly explain the rationale behind the patentee's proposals for category, comparator drug products and where applicable, comparable dosage regimens, making appropriate reference to the relevant Guidelines, Policies and Procedures set out in the PMPRB's Compendium. References used to derive comparable dosage regimens should be identified.
- 6.4 Patentees are encouraged to use the format recommended in [Schedule 8](#) to summarize the information requested in paragraphs 6.2 and 6.3.
- 6.5 The patentee should provide multiple copies of the product monograph, submission and supporting references to Board Staff. The number of copies depends on the proposed category of the new drug product ([refer to Schedule 8](#)).
- 6.6 This material will assist Board Staff in its review of a new drug product. Furthermore, the provision of this information along with either the notification of intended sale ([Schedule 6](#)) or with the filing of Form 1 for the drug product, can expedite the review process by eliminating delays caused by the need to request this information from the patentee at a later date.

## 7. Submissions for Category 2 New Drug Products

- 7.1 In addition to the information outlined in Section 6, patentees wishing to have new drug products considered for Category 2 classification should provide additional information in support of their claim.
  - a. Copies of up to five references to include (if available):
    - A minimum of two well controlled, double-blind, statistically sound clinical trials which compare the new drug product to standard medicines whose value in the treatment of the disease is well recognized;
    - Published reviews in recognized journals of the performance of the drug product or of the class of drug.
  - b. A list of additional references. A complete Medline search on clinical trials and reviews is helpful.

## **Increased Efficacy**

- 7.2 Evidence considered to determine if a medicine provides increased efficacy should derive from well controlled, double-blind, statistically sound clinical trials that compare the new drug product against placebo therapy or standard medicine whose value in the treatment of the disease under consideration is well recognized. All endpoints must be well defined and the means to measure them clearly described and, if necessary, scientifically defended.
- 7.3 Depending upon the therapeutic class involved, the well-defined endpoints are parameters (e.g., Hamilton scale, fever, blood pressure) related to a good clinical practice for the treatment of a specific disease. The parameters selected should reflect the increased efficacy of the new drug product.
- 7.4 Generally, trials should be published in recognized, peer-reviewed journals. Papers documenting the results of these trials will be subsequently reviewed by the HDAP and, if necessary, by sub-specialists for evidence of the increased efficacy of the new drug product as compared to previously available medications.
- 7.5 Published reviews of the performance of the new drug product in recognized journals can also be submitted as evidence of its overall efficacy. These too, will be subjected to the scrutiny of the HDAP.

## **Major Reduction in Dangerous Adverse Reactions**

- 7.6 Evidence considered to determine if a medicine provides reduced toxicity should derive from well controlled, double-blind, statistically sound clinical trials that compare the new drug product against the available standard medicine(s) used to treat the disease or condition under review. The means by which the adverse effects of the new product were measured and their relevance to patient well-being must be described and, if necessary, defended. The evidence of reduced toxicity should be reflected by a diminution of the incidence, the degree and/or the severity of the adverse reactions.
- 7.7 As in the case of data to support evidence of increased efficacy, trials supporting claims of reduced toxicity for the new drug product should also be published in recognized, peer-reviewed journals. Papers documenting the results of these trials will be subsequently reviewed by the HDAP for evidence of reduced toxicity of the new drug product compared to other available medications.
- 7.8 Published reviews of the performance of the new drug product in recognized journals can also be submitted as evidence of its reduced toxicity compared to standard medications. These too, will be subjected to the scrutiny of the Board's Drug Advisory Panel.
- 7.9 When up-to-date product monographs are available for comparator medicines, such monographs will be compared with the product monograph of the new drug product for a listing of the Contra-indications, Precautions, Adverse Effects and Drug Interactions.

## 8. Procedures for Categorization

- 8.1 New drug products will be referred to the HDAP where:
- the new medicine is a new active substance;
  - the patentee submits scientific evidence;
  - uncertainty exists on the part of the staff regarding the appropriate category; or
  - clarification is required on other scientific evaluation issues.
- 8.2 Only the Drug Advisory Panel may recommend that a new drug product be considered a breakthrough or substantial improvement (Category 2).
- 8.3 If a patentee wishes the panels or Board Staff to consider evidence supporting scientific claims, the patentee should submit such evidence in advance of the review of the introductory price (i.e., prior to the date when price data must be filed for the first day of sales).
- 8.4 Recommendations on category submitted by the panel and by Board Staff include the following:
- for *Category 1* drug products, the identification of comparable dosage forms of the medicine and other factors as may be necessary for the purposes of a Reasonable Relationship Test.
  - for *Category 2* and *Category 3* drug products the identification of comparable drug products and comparable dosage regimens as required by the PMPRB's Excessive Price Guidelines for the purposes of a Therapeutic Class Comparison Test.

## 9. Selection of Comparable Drug Products

- 9.1 Comparable drug products are selected by identifying both comparable medicines and comparable dosage forms.

### Comparable Medicines

- 9.2 Comparable medicines are clinically equivalent in addressing the approved indication that is anticipated to be the primary use of the new drug product under review. The PMPRB refers to the World Health Organization (WHO) Collaborating Centre for Drug Statistics Methodology's Anatomical Therapeutic Chemical Classification System (ATC) as the starting point for the selection of comparable medicines.
- 9.3 Comparable medicines will typically be those identified under the ATC classification system at the sub-class level above the single chemical substance. This will normally be the fourth sub-class level. If the appropriate comparable medicines are not identified at this level, then the PMPRB may choose from the next higher sub-class or another sub-class. In some instances, it may be appropriate to select from the fifth or single chemical substance level. Selection criteria will include the indication and therapeutic use, and could include other factors such as mode of action, spectrum of activity or chemical family.
- 9.4 The PMPRB may omit from the comparison a chemical substance or a drug product of the same ATC therapeutic class as the drug product under review if, in the panel's or Staff's opinion, it is not clinically equivalent or is unsuitable for comparison. For example, drug products with primary uses other than to address the indication anticipated to be the primary use of the drug product under review may be omitted from the comparison. Similarly, the PMPRB may choose to add products from other ATC classes if they are clinically equivalent for the appropriate indication to the drug product under review.

## **Comparable Dosage Forms**

- 9.5 For each comparable medicine identified, drug products of the same or comparable dosage form as the drug product under review will generally be selected. [Schedule 7](#) lists the comparable dosage forms that the PMPRB uses to identify comparable drug products.
- 9.6 When comparable dosage forms cannot be identified, other dosage forms may be used if these dosage forms address the appropriate indication and have a clinically equivalent effect.

## **10. Selection of Comparable Dosage Regimens**

- 10.1 The dosage regimen recommended for comparison purposes will normally not be higher than the maximum of the usual recommended dosage taking into account relevant clinical variables. The most appropriate strength of the medicine will be chosen for a particular dosage regimen.
- 10.2 Generally, a dosage regimen based on a course of treatment will be applicable to acute indications, while a per-day regimen (based on maintenance dose) will be applicable to chronic situations.
- 10.3 Board Staff and the panel may rely on product monographs, credible scientific literature, expert advice or any combination thereof to facilitate their recommendation of the maximum of the usual recommended dosage, relevant clinical variables, clinically equivalent effects and other matters relating to price measurement

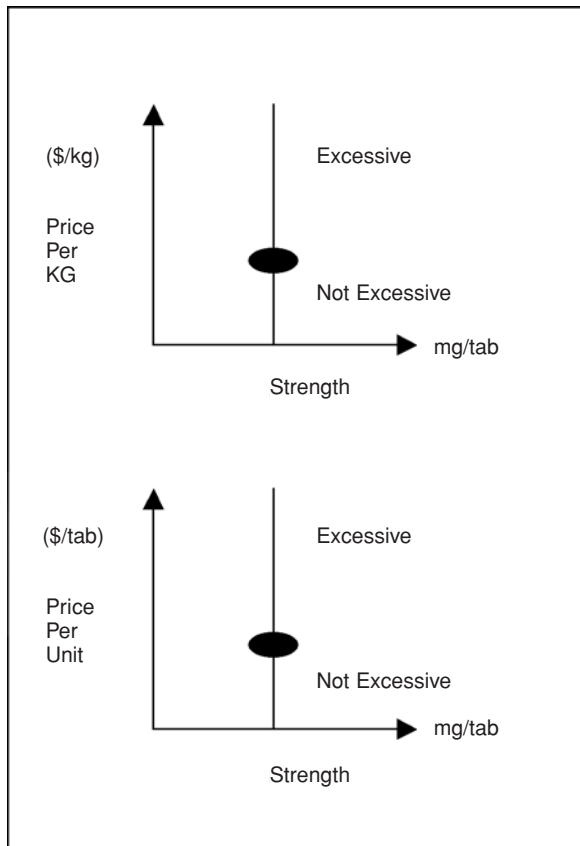
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## Schedule 1 – Reasonable Relationship Test

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Reasonable relationship refers to the association between strength (i.e. commonly expressed in milligrams of active ingredient) and price. The reasonable relationship test defines a maximum non-excessive introductory price for the new DIN. This section describes in general terms the process by which reasonable relationship may be determined.

The determination of reasonable relationship will be based on one of three possible tests. Only one test will be appropriate for a particular new drug product.



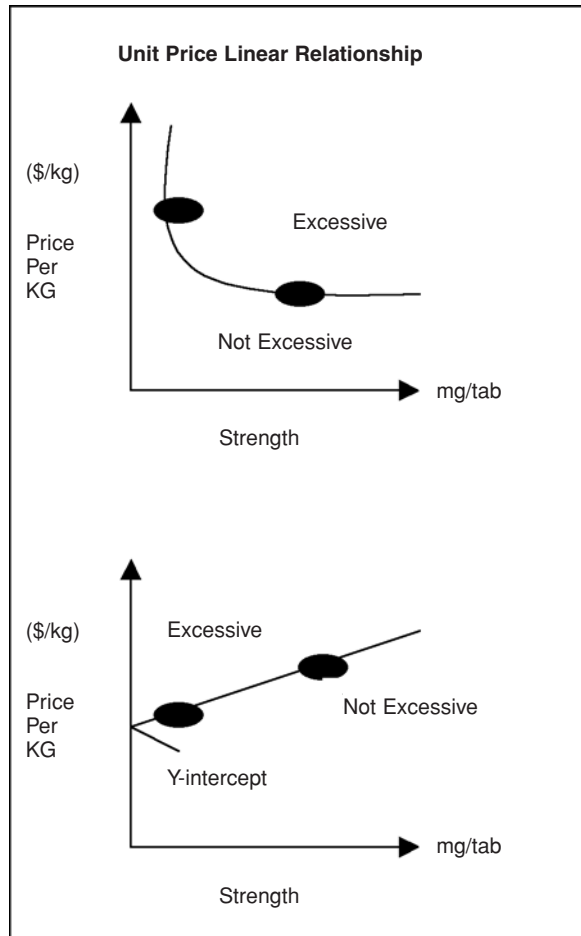
To determine which test is appropriate for a particular case, the three are considered in descending order. The purpose of these tests is to calculate a maximum non excessive price for the new DIN.

### Test 1: Same Strength Test

If there are one or more comparable DIN's of the same strength as the new DIN, then the highest priced comparable DIN of the same strength determines the maximum non excessive price for the new DIN. Prices above this threshold are considered to be outside the PMPRB's Guidelines. The result of this test takes precedence over the other two tests, regardless of their outcomes.

## Test 2: Unit Price Linear Relationship Test

This test is used where there are two or more comparable DIN's and none are the same strength as the new DIN. The test attempts to establish a positive linear relationship between unit prices and strengths of the comparable DIN's. To be acceptable, the linear relationship must have two important properties. First, it must define prices that are positive (i.e.  $> 0$ ) for all possible strengths. Second, the prices of all comparable DIN's must fall on or below the line defined by the linear relationship.



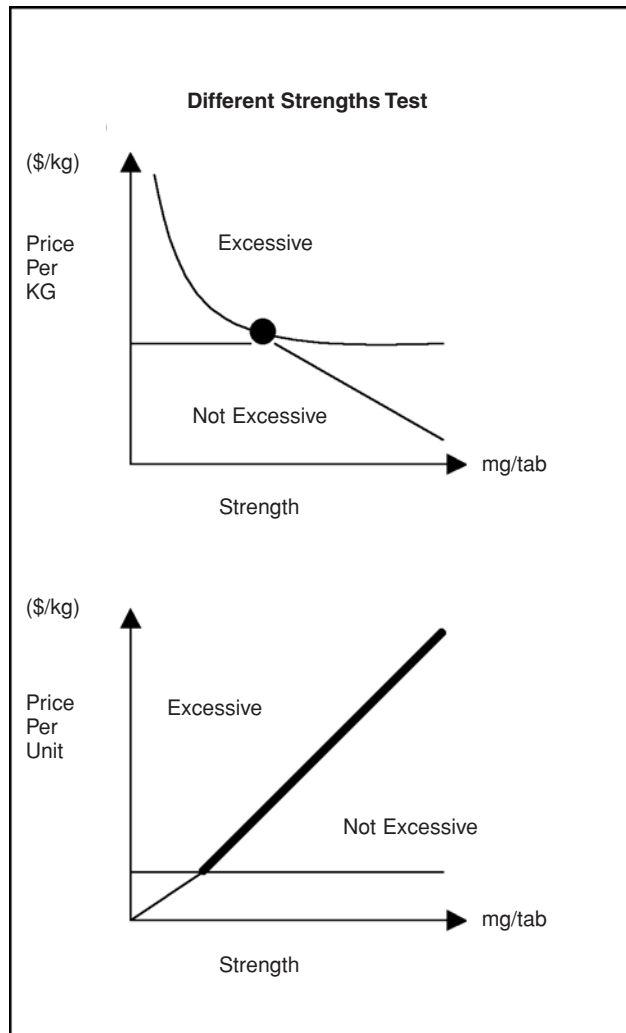
If it is not possible to conduct Test 1 (same strength), and, there are two or more comparable DIN's, the pricing pattern of these comparable DIN's is considered to determine if a unit price linear relationship can be established. Where a positive relationship can be established, it determines the threshold (i.e. maximum non excessive price) above which prices are considered to be outside the PMPRB's Guidelines. Prices at or below the threshold are considered to be within the PMPRB's Guidelines.

To conduct the test, the linear relationships (in price/unit) of all possible pairs of comparable DINs are examined. The pair with a positive slope and highest Y intercept determine the Y intercept of the reasonable relationship line, (i.e. maximum non excessive price threshold). This line is defined to be the line passing through that Y intercept and the point representing the comparable DIN with the highest price/unit. The result of this test takes precedence over the result of test 3, regardless of the latter's result.

## Test 3: Different Strength Test

This test is used if it is not possible to use either of the previous tests (e.g. if there is only one comparable DIN and it is a different strength).

The first step is to locate the comparable DIN with the highest price/unit of active ingredient. The price of the new DIN under review is then considered in relation to the highest price of the comparable DIN.



The critical comparable DIN establishes the maximum non excessive price for the new DIN in one of two ways:

1. If the new DIN is of a higher strength (relative to the strength of the critical comparable DIN), the maximum non excessive price for the new DIN is the price/unit of active ingredient of the critical comparable DIN.
2. If the new DIN is of a lower strength (relative to the critical comparable DIN), the maximum non excessive price for the new DIN is the price/unit of the critical comparable DIN.

### Higher Strength

The price of the new DIN will be outside the Guidelines if the new DIN is of a higher strength and is priced higher than the (\$/kg) price of the comparable DIN with highest (\$/kg) price.

### Lower Strength

The price of the new DIN will be outside the Guidelines if the new DIN is of a lower strength and is priced higher than the (\$/unit) price of the comparable DIN with the highest (\$/kg) price.

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# Schedule 2 – Therapeutic Class Comparison Test

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## 1. Approach

The therapeutic class comparison compares the price of the drug product under review with the price of drug products that are clinically equivalent and sold in the same market at prices that the PMPRB considers not to be excessive. Comparable drug products are first selected and then their prices are compared against the drug product under review.

## 2. Selection of Comparable Drug Products

The identification of comparable drug products is a function of the scientific review process. The selection is comprised of two elements:

- the identification of comparable medicines; and
- comparable dosage forms.

For complete details on the selection of comparable drug products, please refer to [Chapter 3: Scientific Review Procedures](#).

## 3. Measuring the Price

The PMPRB considers it appropriate to compare the prices of comparable drug products taking into consideration the dosage regimen and other clinically relevant variables required to produce a clinically equivalent effect. The PMPRB will make these price comparisons in terms of the price per day or price per course of treatment, whichever is more applicable. Generally, the price per course of treatment will be applicable to acute indications, whereas price per day (based on maintenance dose) will be applicable to chronic situations.

The dosage regimens for both the drug product under review and the comparable drug products to be used in the Therapeutic Class Comparison Test are recommended by the appropriate Drug Advisory Panel and by Board Staff. For further details on this process, please refer to [Chapter 3: Scientific Review Procedures](#).

Ordinarily, the introductory price of the new drug product and the Ontario Drug Benefit Formulary price of the comparable drug products, if available, will be used for the comparison. If the ODB price is not available, or the PMPRB considers it inappropriate, other prices may be used for the comparison. For example, when an identified comparable drug product is patented and marketed by the same patentee as the drug product under review, the comparable drug product's average price based on the patentee's submission to the PMPRB (or, if outside the Guidelines, its maximum non-excessive price) may be used for the comparison.

The PMPRB reserves the right to exclude from the therapeutic class comparison test any drug product it has reason to believe is being sold at an excessive price.



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# Schedule 3 – International Price Comparison

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## 1. Concept

The general objective of the international price comparison is to compare the price of the DIN under review with the prices of the same dosage form and strength of the medicine sold in the countries listed in the [Patented Medicines Regulations](#) (the Regulations).

## 2. Methodology

- 2.1 Whenever possible, the price of the drug product under review will be compared with the simple average of the ex-factory prices of the same strength and dosage form for each country listed in the Regulations (France, Germany, Italy, Sweden, Switzerland, the United Kingdom and the United States).
- 2.2 When a direct comparison of the drug product under review is not possible for a given country, the most similar strengths of comparable dosage forms per [Schedule 7](#) will be considered.
- 2.3 When the International Price Comparison is being conducted to determine the median price and the drug product is sold in an even number of countries, the median will generally be the simple average of the middle two prices.
- 2.4 When the International Price Comparison is being conducted to determine the median price, an interim median international price will be used in cases when the medicine is sold in fewer than five countries at the time of its introduction. Unless it is excessive, the introductory price will be treated as the interim benchmark price. The interim benchmark price may be reviewed at the end of three years or when the medicine is sold in at least five countries, whichever comes first.

## 3. Exchange Rates

- 3.1 In order to apply the highest-price Guideline outlined in [section 7.1 of Chapter 1: Excessive Price Guidelines](#), the exchange rates used are ordinarily the simple average of the thirty-six monthly average noon spot exchange rates for each country (taken to eight decimal places), as published by the Bank of Canada for the thirty-six months ending with the last month of the pricing period under review.

e.g.: The pricing period under review is July to December 1993. The exchange rates used, for the purposes of the highest-price Guideline, are for the months of January 1991 through December 1993.
- 3.2 To review the introductory price of a new drug product, the exchange rates used are the simple average of the thirty-six monthly average noon spot exchange rates for each country (taken to eight decimal places) as published by the Bank of Canada for the thirty-six months ending four months before the date of the first sale of the drug product.

e.g.: If the new drug product under review was first sold in October 1993, the exchange rates used are for the months of June 1990 through May 1993.

3.3 The Guidelines provide that under certain exceptional circumstances, it may be appropriate to review a benchmark price. In such a case, the exchange rates used are ordinarily the simple average of the thirty-six monthly average noon spot exchange rates for each country (taken to eight decimal places), as published by the Bank of Canada for the thirty-six months ending four months before the new benchmark period.

e.g.: The new benchmark period for the drug product is May to June 1993. The exchange rates used are for the months of February 1990 through January 1993.

3.4 In the course of an investigation, the PMPRB may conduct retrospective price reviews. In these cases, the exchange rates used are ordinarily the simple average of the thirty-six monthly average noon spot exchange rates for each country (taken to eight decimal places) as published by the Bank of Canada for the thirty-six months ending with the last month of the pricing period under review.

e.g.: The pricing period under review is July to December, 1993. The exchange rates used, for the purposes of an investigation, would be for the months of January 1991 through December 1993.

## 4. Publication

[Exchange rates](#) are published on the PMPRB web site on a monthly basis, under Frequently Requested Items.

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# Schedule 4 – CPI-Adjustment Methodology

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## 1. The Guideline

- 1.1 The price of an existing drug product during the year under review will be presumed to be excessive if it exceeds the benchmark price of the DIN adjusted for the cumulative change in the Consumer Price Index (CPI) from the benchmark year to the year under review (CPI-adjusted price).
- 1.2 In addition, one year price increases may not exceed 1.5 times the forecast change in the annual CPI.
- 1.3 In periods of high inflation (over 10%), the limit will be five percentage points more than the forecast change in the annual CPI.

## 2. Terminology

- 2.1 Forecast Period: The forecast period is the year for which prices are being set.
- 2.2 Benchmark year:
  - a. For patented drug products first marketed in Canada more than three years prior to the forecast period, the benchmark year is the calendar year three years preceding the forecast period. For example, for 1999, the corresponding benchmark year is 1996.
  - b. For patented drug products first marketed three years or less prior to the forecast period, the benchmark year is the year in which the drug product was introduced in Canada.
- 2.3 Introductory Period

The introductory period for new drug products is the period from the date of first sale to the end of the six-month regulatory reporting period (i.e. June 30 or December 31) when that period is greater than one month. For example, a drug product first marketed in March 1997 would have an introductory period of March to June 1997 whereas a drug product first marketed in October 1997 would have an introductory period of October to December 1997.
- 2.4 Benchmark Price:
  - a. For patented drug products first marketed in Canada more than three years prior to the forecast period, the benchmark price is its average transaction price (ATP) based on the patentee's [Form 2](#), Block 4 submission (or if that price was outside the Guidelines, the maximum non-excessive price) in the benchmark year.
  - b. For patented drug products first marketed three years or less prior to the forecast period, the benchmark price is its ATP based on the patentee's [Form 2](#), Block 4 submission (or if that price was outside the Guidelines, the maximum non-excessive price) during its introductory period. This benchmark price establishes the maximum non-excessive price for the benchmark year.
- 2.5 Base CPI:

The average of the monthly CPI figures, as published by Statistics Canada, for the benchmark year. The base CPI figures are calculated and published annually by the PMPRB [in April].

#### 2.6 Forecast CPI:

The forecast of the CPI figure relevant to the forecast period is based on the previous year's actual CPI published by Statistics Canada and adjusted for the latest annual inflation projections by the federal Department of Finance. The PMPRB's forecast CPI is calculated several months prior to the beginning of the forecast period and published annually [in March].

In February of 1998, Statistics Canada updated the base year of the CPI from 1986 to 1992. Historical rates of growth of the CPI have not been affected by this change in base years. The PMPRB will be adopting the new series in its calculations. The change in base years will not affect CPI-adjustment factors previously published or the calculations of any maximum non-excessive prices. The PMPRB does not anticipate any impact upon patentees of this change of series. Should patentees require more detailed information regarding the change they may refer to Statistics Canada Catalogue No. 62-001 Vol 76 #8 page iv or contact the compliance officer assigned to their companies.

#### 2.7 CPI-Adjustment Factor:

The forecast CPI divided by the base CPI, rounded to three decimal places.

#### 2.8 CPI-Adjusted Price:

The benchmark price multiplied by the CPI-adjustment factor.

#### 2.9 Cap:

One year price increases may not exceed 1.5 times the forecast change in the annual CPI. In times of high inflation (greater than 10%), the limit will be 5 percentage points more than the forecast change in the CPI.

### **3. Information on CPI Adjustment Factors and Forecast CPI**

The CPI Adjustment Factors and Forecast CPI are updated on an annual basis for future pricing periods. The information is published in the NEWSletter and is available on the PMPRB web site under [Frequently Requested Items](#).

## Examples of the Calculation of the CPI-Adjusted Price Using CPI with 1992 as a Base Year

### EXAMPLE 1

Drug Products First Marketed in Canada before January 1, 1995

First Sale: Jan 2 1989

Benchmark year: 1997

Benchmark Price: \$0.2361/tablet

Forecast Period: Jan – Dec 2000

- In this example, the benchmark year is 1997, i.e. the year three years prior to the forecast period. Referring to the benchmark year 1997 (column 1 of the Table 1), the base-CPI (1992=100) is 107.57. The benchmark price is the average price of the patented drug product (or, if that price is outside the Guidelines, the maximum non-excessive price) in the benchmark year.
- Table 1 indicates that the forecast CPI(1992=100) for 2000 is 111.91.
- Calculate the CPI-adjustment factor by dividing the forecast CPI by the base CPI rounded to three decimal places. In this case, the CPI-adjustment factor is  $111.91 / 107.57 = 1.040$  as shown in column 1 of Table 1.
- Calculate the CPI-adjusted price by multiplying the benchmark price by the CPI-adjustment factor. In this case, the CPI-adjusted price for 2000 is  $\$0.2361 \times 1.040 = \$0.2455$ .

### EXAMPLE 2

Drug Products First Marketed in Canada after December 31, 1994

First Sale: Mar 10 1998

Introductory Period: Mar – June 1998

Benchmark year: 1998

Benchmark Price: \$2.0250/ml

Forecast Period: Jan – Dec 2000

- In this example, the benchmark year is 1998, i.e. the year in which the drug product was first sold in Canada. Referring to the benchmark year 1998 (column 2 of Table 1), the base-CPI is 108.63. The benchmark price is the average price of the drug product (or, if that price is outside the Guidelines, the maximum non-excessive price) in the introductory period.
- Table 1 indicates that the forecast CPI for 2000 is 111.91.
- Calculate the CPI-adjustment factor by dividing the forecast CPI by the base CPI rounded to three decimal places. In this case, the CPI-adjustment factor is  $111.91 / 108.63 = 1.030$  as shown in column 2 of Table 1.
- Calculate the CPI-adjusted price by multiplying the benchmark price by the CPI-adjustment factor. In this case, the CPI-adjusted price for 1998 is  $\$2.0250/\text{ml} \times 1.030 = \$2.0858/\text{ml}$ .

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## **Schedule 5 – Criteria for Commencing an Investigation**

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The PMPRB's Compliance and Enforcement Policy provides that the Board may establish criteria for identifying cases for investigation from time to time. The criteria, which are subject to change, may include the amount by which a price exceeds the Guidelines and the amount of excess revenues along with other factors.

The criteria balance the need for pricing flexibility on the part of patentees with the PMPRB's mandate of protecting consumers by ensuring that the prices of patented drug products are not excessive. The Board publishes its criteria for commencing an investigation to improve transparency and to provide patentees with greater certainty as to their responsibilities in the regulatory process.

A price is considered to be within the Guidelines unless it meets the criteria for commencing an investigation. The criteria represent the standards the Board applies in order to allocate its resources to investigations as efficiently as possible. Their existence should not be construed as indicating that the Board accepts any deviation from the Guidelines. The Board is satisfied that its criteria assure all significant cases of pricing outside the Guidelines will be subject to an investigation. In most instances where a price exceeds the maximum allowable price by an amount too small to trigger an investigation in one year, it is offset by a price below that which is permitted by the Guidelines the following year. The Board expects the prices of all patented medicines to be within the Guidelines and evidence of persistent pricing outside the Guidelines, even by a small amount, may be used as a criterion for commencing an investigation.

Should the price of a patented drug product, or its cumulative excess revenues ever meet the criteria, an investigation will be initiated in conformity with the Compliance and Enforcement Policy. If the investigation confirms that the price exceeds the Guidelines, the patentee may choose to voluntarily adjust its price and offset the excess revenues through a Voluntary Compliance Undertaking (VCU).

Patentees will be advised of cumulative excess revenues for each of their DIN's as part of the compliance reports they receive from the PMPRB. Excess revenues below the amount specified in the criteria can be reduced voluntarily by the patentees in subsequent years by pricing below the maximum non-excessive price. However, cumulative excess revenues cannot fall below zero.

## **Criteria for Commencing an Investigation**

Board Staff will commence an investigation into the price of a patented drug product when any of the following criteria are met:

### **New Drug Products**

1. The introductory price is 5% or more above the maximum non-excessive price;
2. Excess revenues in the introductory period are \$25,000 or more; or
3. Complaints with significant evidence.

### **Existing Drug Products**

1. A price is 5% or more above the maximum non-excessive price and there are cumulative excess revenues of \$25,000 or more over the life of the patent after January 1, 1992;
2. Cumulative excess revenues are \$50,000 or more over the life of the patent after January 1, 1992; or
3. Complaints with significant evidence.

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## Schedule 6 – Notification of Intent to Sell – Subsection 82(1)

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Pursuant to [subsection 82\(1\) of the \*Patent Act\*](#), patentees are required to notify the PMPRB of an intention to sell a patented medicine in a new market in Canada and the date on which the patentee intends to offer the medicine for sale. Specifically:

*82(1) A patentee of an invention pertaining to a medicine who intends to sell the medicine in a market in Canada in which it has not previously been sold shall, as soon as practicable after determining the date on which the medicine will be first offered for sale in that market, notify the Board of its intention and of that date.*

Pursuant to [subsection 82\(2\)](#), the Board may require a patentee to provide information and documents respecting the price at which the medicine is intended to be sold.

### Information to be Filed

Patentees must notify the PMPRB as soon as practicable after determining the date on which the medicine will first be offered for sale in Canada. As the PMPRB reviews the average prices of each patented medicine sold in Canada, it will normally be sufficient to notify the PMPRB with reference to the introduction of the product in Canada and not on each subsequent occasion when it is to be introduced in a new market.

Information should be filed for each drug product (DIN) – including Investigational New Drugs (IND's) and drug products sold under the Special Access Programme (SAP), which the patentee intends to sell.

For purposes of [subsection 82\(1\)](#), the PMPRB requests patentees to file the following information:

- Brand and Generic name.
- Dosage form and strength.
- Date medicine will first be offered for sale.
- DIN (if available) and NOC date (or anticipated date).
- Canadian Patent Number(s) and name and address of Canadian Patentee.

The form may be used to assist in the provision of the above information to the Board. If a patentee has additional information which it wants considered in reviewing the price, it may wish to file such information when notifying the PMPRB under subsection 82(1). This information might include the product monograph and relevant scientific studies.



**Notification of Intention to Sell a Patented Medicine**  
*(In accordance with [subsection 82\(1\) of the Patent Act](#))*

Brand Name:

Generic or Chemical Name:

Dosage Form:

Strength:

DIN (if available):

Date of NOC (anticipated):

Expected Date of First Sale:

Canadian Patent Number(s):

Name and Address of Canadian Patentee:

Authorized signing officer:

*Signature*

*Name and Title*

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## **Schedule 7 – Comparable Dosage Forms**

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This Schedule is used for purposes of identifying comparable dosage forms in conducting therapeutic class comparisons of new drug products and identifying a drug product in category 1 which is a new DIN of a comparable dosage form of an existing medicine. It should be noted that formulations under each sub-class are considered distinct from another sub-class.

The PMPRB reviews the list of comparable dosage forms periodically to ensure that it includes those currently used.

<b>Comparable Dosage Forms</b>		
<b>Topical</b>	<b>Nasal/Pulmonary</b>	<b>Oral Solid</b>
Aerosol Cream Disks Dressings Egg dip concentrate* Gel Liquid Ointment Paste Patches Powder Shampoo Spray	Aerosol Drops Gas Metered dose preparations Powder Solution Spray	Capsule Effervescent – powder – tablets – granules Food mix* Modified release formulations Tablet
<b>Oral Liquid</b>	<b>Vaginal</b>	<b>Parenteral</b>
Drops Modified release formulations Powder for drinking water* Powder for – solution – suspension Solution Suspension	Cream Cone Douche Foam Gel Insert Ovule Sponge Suppository Tablet Tampon	Implant Modified release injections Powder for solution Solution Suspensions or Emulsions
<b>Otic/Ophthalmic</b>	<b>Rectal</b>	<b>Dental/Sublingual Buccal</b>
Drops Gel Liquid Modified release ocular devices Ointment Powder for solution Suspension	Cream Enema Foam Ointment Suppository Suspension	Gel Gum Lozenge Modified release buccal Mouth wash Powder for suspension Solution Sprays – sublingual – buccal Sublingual tablets Suspension

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## Schedule 8 – Submissions for New Drug Products

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Sections 6 and 7 of the Scientific Review Procedures outline the information that patentees are requested to provide to Board Staff for each new patented drug product, for human and veterinary uses, they propose to market.

This Schedule summarizes the requirements for information, supporting evidence and number of copies of each submission to be provided. Patentees are encouraged to use the format recommended in this Schedule to present the requested information.

### Supporting Evidence Required

	Rationale	Product Monograph*	Published Reviews (3)	Clinical Trials (4)	Medline Search (5)	Number of Copies
Category 1	+(1)	+	–	–	–	3
Category 2	+(1)(2)	+	(+)	+	+	7
Category 3	+(1)(2)	+	–	–	–	4

- + Required
- (+) Required if available
- Not Required

\* Information identifying the medicine shall be accompanied by the product monograph for the medicine or, if a notice of compliance has not been issued in respect of the medicine, by information similar to that contained in a product monograph.

## Notes:

- (1) Rationale for the proposed categorization (max. 1 page) and explanation for the selection of comparator drug products.

**Category 1** products are normally compared to other DINs of the same medicine in comparable dosage forms, generally manufactured by the same patentee (i.e. line extensions). For **Category 2 and 3** products, provide carefully documented rationale for any comparator drug product proposed where:

- the ATC class of the comparator drug product is different from that of the drug product under review;
  - the accepted use of the comparator drug product is not approved for the primary use of the drug product under review, or
  - the comparator drug product is in a non-comparable dosage form according to [Schedule 7 of the PMPRB Compendium of Guidelines, Policies and Procedures](#).
- (2) Rationale and identification of references used to derive the comparable dosage regimens proposed.
  - (3) Published reviews in recognized journals of the performance of the drug product or of the class of drug, if available.
  - (4) Minimum of two and a maximum of 5 well controlled, double blind, statistically sound clinical trials which compare the new drug product to standard medicines whose value in the treatment of the disease is well recognized.
  - (5) A complete Medline search on clinical trials and reviews is helpful. Key words used to conduct the search should be identified.

Attached is the blank form entitled "Submission by patentee for categorization/review of a new drug product by the PMPRB" ([PDF](#) – 15kb).

## Submission by Patentee for Categorization/Review of a New Drug Product by the PMPRB

Company	Brand Name	Generic Name	DIN	Dosage Form	Strength	ATC Code*	Max. Usual* Recommended Dose

\* For primary use

### Approved Indication (s) and Primary Use:

**Proposed Category:**

- (1) Provide reference(s) for the proposed dosage regimen (cross-reference in column REF to attached indexed list of references).
- (2) Indicate if comparator drug products approved for primary use of DIN under review (check mark (√) in column APP'D)

Company	Brand Name	Generic Name	DIN	Dosage Form	Strength	ATC Code*	Max. Usual* Recommended Dose	Ref(1)	App'd(2)

\_\_\_\_\_  
Patentee Medical or Scientific Officer

\_\_\_\_\_  
Date