

Introduction & Background

This response to the Proposed Amendments to the *Patented Medicines Regulations* (the *Regulations*) has been prepared by Neil Palmer, Founder and Principal Consultant of PDCI Market Access Inc. (PDCI). The views expressed are solely those of Neil Palmer & PDCI.

PDCI is Canada's leading pricing and reimbursement consultancy, co-founded in 1996 by Neil Palmer who previously was on the staff of the PMPRB for several years. Mr Palmer is widely acknowledged as an expert on pricing and the PMPRB and has been recognized by the Federal Court of Canada in several cases as an expert in market access, reimbursement policies, and pricing regimes of the Canadian pharmaceutical marketplace. Mr Palmer is also Adjunct Assistant Professor of Pharmaceutical and Health Economics Practice at the University of Southern California¹ where he lectures on pricing, reimbursement and market access.

Potential Conflicts of Interest

Neil Palmer and PDCI have received no financial assistance or any input from the pharmaceutical industry or anyone else in the preparation of this document.

PDCI's clientele is predominantly the innovative pharmaceutical industry. PDCI assists pharmaceutical manufacturers (patentees) navigate the PMPRBs regulations and guidelines and assists patentees with advice when their products are subject to PMPRB compliance and enforcement measures.

Furthermore, PDCI assists patentees with their filing of international prices by sourcing the prices from the PMPRB recognized prices sources, backing out the upcharges and VAT, and compiling the price data on the PMPRB Form-2 Block5- in accordance with the Regulations. Accordingly, PDCI will likely benefit financially (increased revenues from consulting fees) should the list of reference countries be expanded, and/or, the new proposed price factors and reporting requirements be implemented in Regulation.

General Observations

Regulatory Framework. The federal government has established a framework for making and amending regulations. The framework consists of 6 key elements²:

1. Canadians are consulted
2. Risk exists, government intervention is required, regulation is best alternative
3. Benefits of regulation outweigh costs
4. Adverse economic effects are minimized, no unnecessary regulatory burden

¹ <https://hcda.usc.edu/faculty/>

² **Guide to Making Federal Acts and Regulations: Part 3 - Making Regulations, Privy Council Office**
<http://www.pco-bcp.gc.ca/index.asp?lang=eng&page=information&sub=publications&doc=legislation/part3-eng.htm>

5. International and intergovernmental agreements are respected
6. Systems in place to manage regulatory resources effectively

It is not apparent from the proposed *Regulations* and Regulatory Impact Assessment Statement (RIAS) that risks exist given that the PMPRB's own analysis suggests that on average Canadian prices are consistently at or below the international median and that prices have remained flat³ despite guidelines that allow for price increases. And to the extent that any risk exists, it is not evident that government intervention is required, nor that regulation is the best alternative to address the risk.

PMPRB can already consider additional excessive price factors without the proposed Regulations. The *Patent Act* (para 85 (2) (b)) already allows the Board to consider any factor it considers to be relevant in the circumstances, whether or not that factor is in the *Act* or in the *Regulations*:

(2) Where, after taking into consideration the factors referred to in subsection (1), the Board is unable to determine whether the medicine is being or has been sold in any market in Canada at an excessive price, the Board may take into consideration the following factors:

(a) the costs of making and marketing the medicine; and

(b) **such other factors** as may be specified in any regulations made for the purposes of this subsection **or as are, in the opinion of the Board, relevant in the circumstances.**

The Patent Act already allows these and any other factor to be considered by the PMPRB as secondary factors. In addition, the PMPRB has the power to issue orders to require patentees to provide any information necessary to assess a price in the context of any additional factors. In summary, it is not evident that new factors need to be added through regulation or that significant additional regulatory reporting burden be imposed on all patentees when PMPRB can seek the information in the few cases where it is relevant.

Pharmacoeconomics (PE) as an Excessive Price Factor

Comprehensive pharmacoeconomic (also known as health economic or HE) evaluations are currently conducted by the Canadian Agency for Drugs and Technology in Health (CADTH) and the Quebec Institut national d'excellence en santé et en services sociaux (INESSS). These organizations are the preeminent Canadian health technology assessment (HTA) agencies with expertise in the evaluation and interpretation of health economic models. HE evaluations are intended to inform the potential value to payers – to inform reimbursement decisions and price negotiations – but not to set drug prices or price ceilings. Indeed, to our knowledge, health economics is not used to set drug prices anywhere in the world.

The RIAS offers no rationale as to how HE information will be used in the price review process (ie, as part of the PMPRB Guidelines) nor does it justify reassessing analyses already conducted by CADTH and INESSS and duplicating negotiations of the pCPA (possibly with conflicting results).

³ PMPRB Annual Report 2016

The common measure of cost-effectiveness is an incremental cost effectiveness ratio (ICER) expressed as the cost per Quality Adjusted Life Year (or cost per QALY). However, the cost per QALY is not calculated as a single figure but rather as a range given various underlying assumptions, scenarios and the uncertainty of the clinical evidence, cost estimates and quality of life measures upon which the HE analysis is based.

Moreover, there are many limitations to QALY based analyses as they are often not appropriate for acute conditions (eg, pain) or for rare diseases. For rare diseases it is now well established in the literature⁴ and in practice (eg, in the UK) that the cost per QALY should only be used as one of several factors to assess value. The PMPRB proposes to use the cost per QALY as a standalone threshold for limiting drug prices contrary to best practices.

And contrary to assertions in the RIAS, the cost per QALY does not reflect “value of a medicine to a patient” but rather the value to payers. In fact, the true value to patients (timely access to innovative medicines) and the patient perspective is completely ignored in the RIAS.

The RIAS anticipates that the PMPRB will require additional funding (\$2M/year) for hearings as a result of the new excessive price factors (including health economics). PMPRB Hearings are adversarial, quasi-judicial trial-like proceedings where rules of evidence must be respected. Under the proposed regulations PMPRB Staff will rely on reports prepared by CADTH (and/or INESSS) for its HE cost per QALY evidence.

As a primary factor, the CADTH reports will have to be introduced as evidence in all PMPRB excessive price hearings. CADTH staff with direct knowledge of how the reports were prepared will be required to testify as “fact” witnesses for the PMPRB Staff and be subject to cross examination by the patentee’s lawyers and lawyers for any intervenors. The CADTH reports are not prepared with the PMPRB pricing regime in mind and the CADTH authors will likely not appreciate being co-opted as PMPRB witnesses.

Market Size as an Excessive Price Factor

The affordability issue is best addressed by the pan Canadian Pharmaceutical Alliance (pCPA) that negotiates price volume agreements on behalf of all public drug plans in Canada. Indeed, in February 2017, the pCPA managed to negotiate agreements with the manufacturers of six breakthrough hepatitis C drugs to ensure their affordability and sustainability with the drug plans.

Moreover, the assumption that patented medicines are monopolies protected from new entrants is flawed. Increasingly, new patent protected medicines quickly face competition from similar (often better) medicines, particularly where there is a significant patient population that could benefit from treatment. This was the case for hepatitis C where the number of new entrants has been dramatic and the competition intense – competition leveraged by the pCPA to negotiate price volume agreement for

⁴ See for example Annemans et al, “Recommendations from the European Working Group for Value Assessment and Funding Processes in Rare Diseases (ORPH-VAL)” <https://ojrd.biomedcentral.com/articles/10.1186/s13023-017-0601-9>

the entire therapeutic class. The PMPRB mandate is tied to individual drugs and the PMPRB's protracted quasi-judicial legal framework does not lend itself to group price negotiations. Accordingly, the pCPA and not PMRPB is best positioned to address the affordability issue.

Finally, the RIAS refers to the "number of patients that can benefit from a medicine" in their description of "market size" yet the proposed Regulations would have patentees provide the "estimated maximum use of the medicine by the quantity of the medicine in final dosage form". It is not evident how forecasts of sales of tablets and capsules correspond to "number of patients" considering that medicines typically have multiple indications treating multiple patient populations each with a range of dosing. The proposed regulation (forecasts of the medicine in final dosage form) will not address the stated regulatory objective (number of patients that can benefit from a medicine). To achieve that objective the PMPRB staff will have to request additional information from patentees beyond what is included in the proposed Regulations. All information to be requested by patentees must be included in the proposed Regulations and be subject to consultation.

Amending the list of countries used for international price comparisons

Rationale for Amending the List

The rationale for amending the list of reference countries is predicated on the myth that the PMPRB's current price control regime was somehow structured to go easy on patented drug prices in exchange for significant R&D commitments. The upshot being that since R&D expenditures as a ratio to sales have fallen, it is time for the PMPRB to limit Canadian prices to the median of twelve lower priced OECD countries as part of a new suite of punitive pricing regulations and guidelines. The problem is the underling "R&D" premise is a pernicious myth - the PMPRB price control regime was never tied to levels of pharmaceutical R&D.

The selection of the current seven reference countries (PMPRB7) listed in the *Patented Medicines Regulations* were negotiated between government and industry resulting in a balance consisting of some countries with high prices and some with low drug prices.

The starting point was a dozen or so industrialized countries but never the full slate of OECD countries (the starting point for the current PMPRB12). Rather, the task was to create a manageable basket of (say seven) reference countries such that high price countries (which at the time included US, Germany, Denmark, Japan) would be offset by low price countries (which then and now include France, Italy, Spain). Other countries (e.g., UK, Sweden, Switzerland, Belgium, Netherlands) had prices that fell between the high and low-priced markets.

In the end, the post hoc rationale advanced for the PMPRB7 was that the countries selected had R&D to sales ratios to which Canada aspired. The US and Germany were the high-priced countries offset by France and Italy as the low-priced countries with the UK, Sweden and Switzerland rounding out the seven. However, it was never suggested or even implied (as is being suggested today) that in 1988 there was a link between R&D expenditures and high drug prices or that the selection of reference countries and PMPRB's price regulation was somehow tied to the industry's separate Canadian R&D commitment.

If the linkage between increased R&D and high drug price is to be believed, then the industry's "reward" for committing to increased R&D expenditures was to submit to price control legislation that did not exist prior to December 1987.⁵

Selection of the PMPRB12

The RIAS cites three criteria that were ostensibly the basis of selecting the new basket of reference countries. However, it would appear to be no coincidence that the proposed basket of twelve countries (PMPRB12) would result in a median price corresponding to the median of OECD countries (as publicly proposed by the Minister of Health in May 2017⁶ and in previous PMPRB tweets⁷). Accordingly, the three "selection" criteria really appear to be disingenuous, post hoc rationale for justifying the undeclared desired outcome (ie, the OECD median) and not the objective, reasoned approach portrayed in the RIAS.

International Reference Pricing becoming less relevant

It is widely acknowledged that international reference pricing (IRP) is becoming less relevant. Canada was the first country to employ IRP in 1987 with the C-22 amendments to the *Patent Act* that created the PMPRB and the subsequent Regulations (1988) that identified the seven reference countries. Although the *Act and Regulations* have all been amended and updated since, the PMPRB has maintained its approach to IRP until 2016 when PMPRB concluded (in a consultation document) that less reliance should be placed on IRP.

"Given that it is standard industry practice worldwide to insist that public prices not reflect discounts and rebates, should the PMPRB generally place less weight on international public list prices when determining the non-excessive price ceiling for a drug?"⁸

Rather than less important, the PMPRB's Guideline Scoping Paper⁹ makes it clear that IRP will become more relevant with a median international price test (based on the PMPRB12) applied to all new patented medicines as a first step before prices are further lowered by additional excessive price factors.

Removing the US as a reference country creates a situation such that international price comparisons would not be possible for approximately ten per cent of patented medicines. There are price sources in the US market (other than list prices) that may be more representative of actual transaction prices.

⁵ For more detailed discussion on the R&D myth see "PMPRB myth busting (I): The imaginary link between Canadian price controls and R&D expenditures" <http://www.pdci.ca/pmprb-myth-busting-i-the-imaginary-link-between-canadian-price-controls-and-rd-expenditures/>

⁶ Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations <https://www.canada.ca/en/health-canada/programs/consultation-regulations-patented-medicine/document.html>

⁷ See for example https://twitter.com/PMPRB_CEPMB/status/781494933379280897

⁸ PMPRB Guidelines Modernization – Discussion Paper – June 2016

⁹ PMPRB Guidelines Scoping Paper – High Level Overview of Potential New Framework (Canada Gazette, Part I) <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1341>

These include the FSS price already reported by patentees as well as Medicare and Medicaid prices (or average prices) that are widely available on federal and state websites.

There is no analysis offered as to why Switzerland was removed, or why South Korea added to the list of reference countries – again the intended purpose appears to be to drive the PMPRB median to the OECD median (although that rationale was not offered). If it is appropriate to expand the basket of reference countries, it is more appropriate to consider established international groupings of advanced nations with similar economic characteristics. (eg, the G10¹⁰ or G12¹¹)

Adding reference countries adds to the regulatory burden of patentees and the resources required by PMPRB to carry out its mandate. This cost is significantly underestimated in the RIAS and the accompanying Cost Benefit Analysis.¹²

PMPRB has yet to disclose corresponding Guidelines

The PMPRB (belatedly) published its Guidelines Scoping Paper document after the pre-publication of the *Regulations* that offers a conceptual framework but is short on details. To date, the PMPRB has not offered even a single example of how new price guidelines will be applied. Yet they were able to provide Health Canada analysts with sufficient detail to estimate impacts on the Cost Benefit Analysis that was completed in early September 2017. The new guidelines are essential to understanding and assessing the true impacts of the proposed Regulations and providing meaningful feedback on the proposed Regulations.

Recommendations

- Health Canada and PMPRB should retract the proposed amendments to the Regulations and engage in meaningful consultations and negotiations with industry – this is the most efficient and effective way to achieve the government’s objectives and limit unintended consequences (in the same way that pCPA negotiated a pricing framework with generic drug industry)
- Any future amendments to the Regulations to introduce new excessive price factors should be proposed in concert with the new Guidelines that will apply the factors such that all stakeholders can assess the impact and offer meaningful feedback
- Patient groups must be involved throughout the process, not just as an afterthought
- Transparency: Health Canada should disclose all submissions it receives with respect to the proposed amendments

¹⁰ The Group of Ten is made up of eleven industrial countries (Belgium, Canada, France, Germany, Italy, Japan, the Netherlands, Sweden, Switzerland, the United Kingdom and the United States) which consult and co-operate on economic, monetary and financial matters

¹¹ The Group of Twelve or G12 is a group of industrially advanced countries whose central banks co-operate to regulate international finance. (G10 + Spain and Australia)

¹² See the PDCI report “Proposed Amendments To The Patented Medicines Regulations: A Critical Appraisal Of The Cost-Benefit Analysis” http://www.pdci.ca/wp-content/uploads/2018/01/20180129_PDCI-Critical-Assessment-PM-Regs-Amendments_Report-Final.pdf