

Submission on the October 2022 PMPRB Draft Guidelines The Canadian Forum for Rare Disease Innovators (RAREi) December 2022

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1. Introduction

The Canadian Forum for Rare Disease Innovators (RAREi) welcomes the opportunity to offer its feedback on the Patented Medicine Prices Review Board’s (PMPRB’s) 2022 proposed update to its guidelines for patentees.

After a multi-year journey during which the PMPRB has attempted to “modernize its administrative framework,” highlighted by multiple proposals, consultations, legal actions and delays, RAREi was hopeful that the board would propose a measured and minimally interventionist approach to meeting its regulatory mandate – which, as the Federal Court of Appeal confirmed, is limited “to balance the promotion of innovation with measures to protect ... consumers from excessive patented medicines prices.”¹ Unfortunately, that hope proved elusive.

Instead, the PMPRB has proposed guidelines that appear to be designed to aggressively force list prices of new medicines down below the international median, with no explanation for how and why that new benchmark is the appropriate limit between non-excessive and excessive pricing. At the same time, the proposed guidelines provide patentees with no clarity regarding what a compliant price might be and give PMPRB staff almost unlimited discretion to determine when and how a product should be investigated and considered for a hearing recommendation.

¹ Federal Court of Canada decision, *Innovative Medicines Canada et al. v The Attorney General of Canada et al*, para. 89, June 29, 2020: https://www.smartbiggar.ca/docs/default-source/rx/t-1465-19-final-decision.pdf?sfvrsn=1fa73c56_2.

In presenting the new draft guidelines, board staff claimed that it remains intent on pursuing its “consumer protection” mandate and is aligning with the case law that has evolved recently about the PMPRB’s scope and mandate.

However, in the federal court’s 2020 decision in response to *Innovative Medicines Canada et al’s* request for a judicial review of proposed *Patented Medicines Regulations*, the court stated clearly that “Parliament never intended for the Board to set prices” ... and “the Board is not empowered to control or lower prices absent a finding of excessive pricing.”² More specifically, the Federal Court of Appeal stated in a recent decision related to a PMPRB finding of excessive pricing that “the Board has misunderstood the mandate Parliament has given to it,” pointing out “that the excessive pricing provisions in the *Patent Act* are directed at controlling patent abuse, not reasonable pricing, price-regulation or consumer protection at large.” It also explicitly rejected the board’s interpretation that it has a “consumer protection” mandate.³

At some level, it should probably come as no surprise that the board is proposing measures that aim to reduce patented medicine prices in Canada despite the court’s direction. That is because during the past several years of federal price review reforms, the PMPRB has consistently disregarded the input provided by researchers, health professionals, patients, the innovative pharmaceutical industry and Canada’s two largest provinces. There have been consistent studies, analysis and warnings that the PMPRB’s focus on reducing Canadian list prices of patented medicines have already reduced this country’s attractiveness as a place to launch new innovative treatments, and that this trend will continue as in the face of the PMPRB’s operational plan.

For example, Nigel Rawson’s analysis (supported by RAREi) in *Canadian Health Policy* reviewed the effects of the change in countries on rare disease medicines, and specifically global decisions about whether and at what price to launch a new medicine in Canada. Dr. Rawson concluded that a rare disease medicine’s price would have to be reduced significantly and the uncertainty regarding a compliant price would likely result in an innovator taking a wait and see approach to launching the product. Launches of new medicines in Canada will, at best, be delayed and, at worst, not happen in order to protect the price in markets that are bigger and more profitable.⁴

In spite of board staff’s consistent insistence that product pricing has no discernible effect on launch decisions, the data demonstrating a link is quite compelling.

For example, a Life Sciences Ontario-sponsored IQVIA review of Canada’s performance in launching new treatments compared to other countries over time revealed that between 2017 and 2021, there were an annual average of 34 new medicines launched globally but an average of just 20 per year in Canada. It also found that Canada in 2021 experienced the longest time to

² Ibid. para. 85.

³ Federal Court of Appeal decision, *Alexion Pharmaceuticals Inc. v Canada (Attorney General)*, paras. 49-51, July 29, 2021: <https://decisions.fca-caf.gc.ca/fca-caf/decisions/en/item/500849/index.do>.

⁴ Rawson N et al, *Effect of amended Patented Medicine Regulations on industry decisions to launch new drugs in Canada*, Canadian Health Policy, July 13, 2022: <https://www.canadianhealthpolicy.com/product/effect-of-amended-patented-medicine-regulations-on-industry-decisions-to-launch-new-drugs-in-canada>.

launch new medicines since 2012. New treatments launched in 2021 experienced a median delay after the first global launch of 2.1 years.⁵

The PMPRB's own data confirmed the recent trend of falling numbers of new product launches. Its recent annual report indicated that 2021 saw the fewest number of new patented medicines (59) reported to the board during the year since its inception. More starkly, the 59 new entrants in 2021 compared with 79 in 2020, 81 in 2019 and 108 in 2018, demonstrating a clear and consistent reduction during the course of the board's modernization efforts.⁶

This trend seems at odds with several recent federal government policies that are clearly directed at improving access to medicines and growing the life sciences sector in this country. In fact, when federal Health Minister announced the most recent amendments to the *Patented Medicines Regulations* in April, he stated "the Government of Canada is committed to improving access to quality medicines for Canadians."⁷ In addition, during the past few years, the government has undertaken consultations related to the development of a new pan-Canadian genomics strategy and a national rare disease treatment strategy and launched a national biomanufacturing and life sciences strategy.

Among the key objectives of the developing genomics strategy is "driving the commercialization and use of Canadian genomics technology and innovations and adopting genomics in key sectors, including health care".⁸ The stated purpose of the national rare disease treatment strategy is to "help Canadians with rare diseases access the drugs they need."⁹ Finally, one of the five pillars of the federal biomanufacturing and life sciences strategy is enabling innovation by ensuring world class regulation in order to make Canada a more attractive destination for leading life sciences firms to establish and grow.¹⁰

The PMPRB's proposed efforts to push prices of innovative medicines down and actively discourage the launch of new innovations in Canada would undermine each of those policy initiatives and therefore must be reconsidered with those objectives in mind.

⁵ Life Sciences Ontario, *Is Canada losing its status as a priority medicine launch country?* June 10, 2022: https://lifesciencesontario.ca/is-canada-losing-its-status-as-a-priority-medicine-launch-country-preview_id6648preview_nonce0772186744previewtrue.

⁶ PMPRB 2021 Annual Report, pp. 16-17, September 15, 2022; <https://www.canada.ca/content/dam/pmprb-cepmb/documents/reports-and-studies/annual-report/2021/2021-Annual-Report-en.pdf>

⁷ Health Canada, *Statement from minister of health on the coming-into-force of the regulations amending the Patented Medicines Regulations*, April 14, 2022: <https://www.canada.ca/en/health-canada/news/2022/04/statement-from-minister-of-health-on-the-coming-into-force-of-the-regulations-amending-the-patented-medicines-regulations.html>.

⁸ Innovation, Science and Economic Development Canada, *Government of Canada launches consultations on the development of the Pan-Canadian Genomics Strategy*, May 24, 2022: <https://www.canada.ca/en/innovation-science-economic-development/news/2022/05/government-of-canada-launches-consultations-on-the-development-of-the-pan-canadian-genomics-strategy.html>.

⁹ Health Canada Consultation Notice, *National Strategy for Drugs for Rare Diseases Online Engagement*. July 26, 2021: <https://www.canada.ca/en/health-canada/programs/consultation-national-strategy-high-cost-drugs-rare-diseases-online-engagement.html>

¹⁰ Innovation, Science and Economic Development Canada, *Canada's Biomanufacturing and Life Sciences Strategy*, July 28, 2021: <https://ised-isde.canada.ca/site/biomanufacturing/en/canadas-biomanufacturing-and-life-sciences-strategy>.

The board’s job is to ensure that Canadian prices of patented medicines are not “excessive.” RAREi contends that obliging or forcing innovators to price below the median of comparable countries and therapeutic classes are out-of-scope for the PMPRB. In addition, its policy goals are in direct conflict with other federal policy positions.

As such, the draft guidelines should be abandoned and replaced with a more minimalist and balanced approach to price regulation that is more consistent with the PMPRB’s intended mandate – to ensure that patentees are not abusing their rights by pricing products excessively during a period of market exclusivity.

2. Creating pricing uncertainty

One of the more concerning aspects of the PMPRB’s proposed new approach is the uncertainty that it creates for patentees. That uncertainty is evident in a variety of ways.

The first issue is the PMPRB’s decision to abandon its traditional approach to price review. Up until now, the board has applied guidelines in a manner that helps establish an acceptable “non-excessive average price” or NEAP for a given product using a series of price tests. This model has allowed patentees to predict with relative certainty what would be a compliant price in their business planning.

The shift to a criteria-based investigation model that might or might not lead to an investigation is highly problematic. That is because innovators are prevented from determining with any certainty what might be a compliant Canadian price. This lack of clarity makes it impossible to project future economic results in this market and puts prices of the same product in other markets, where Canadian prices are referenced, at risk.

In addition, the extraordinary discretion the board would give to staff to determine comparators and whether to commence an investigation leaves too much room for interpretation and puts innovators in a constant state of potential jeopardy if, at any point, the product in question is determined by staff to run afoul of the established criteria or an investigation is commenced due to any complaint.

This is particularly concerning for rare disease innovators given that RAREi members have disproportionately been the target of PMPRB investigations in recent years. In addition, the board has been making the case publicly during the past several years that “expensive drugs for rare diseases” or EDRDs have been largely driving the growth in medication costs for the past several years. Despite reporting moderate annual rates of patented medicine sales growth during the past decade, and that fact the percentage of total medications sales in Canada represented by medicines subject to PMPRB jurisdiction was lower in 2021 than at any time since 1997, the PMPRB’s 2021 annual report emphasized that high-cost treatments were the main driver of medication cost increases. It noted that the top-20 medicines (39.6% of patented medicine sales) had a median annual treatment cost of \$42,616 in 2021, nearly 60 times the median in 2012.¹¹

¹¹ PMPRB 2021 Annual Report, pp. 31-38.

That suggests to RAREi members that the board staff are likely to be very focused on higher priced treatments and inclined to give them more attention in their determinations of which products should be subjected to investigations.

In addition, RAREi members have had negative experiences in dealing with PMPRB staff where therapeutic comparators used to support price review investigations have included inappropriate or irrelevant comparators, absent clearly defined scientific evidence evaluation methods and questioned by clinical experts. These experiences do not bode well for a scenario in which the PMPRB staff will have considerably more discretion in assessing compliant pricing. Alternatively, RAREi requests that independent, arms-length expert clinicians should be called upon to determine what the appropriate comparator ought to be. RAREi believes that those expert opinions should be binding on PMPRB staff and the board.

Moreover, the reliance on a floating median as an investigation criteria is also of great concern. Inevitably, prices will have to be altered as the relevant therapeutic class evolves, exchange rates move and prices in comparison countries change, often reflecting negotiated net prices (e.g. Germany). This will require regular and disruptive revisions to the Canadian price and will create scenarios where a product may be subject to multiple investigations as the pricing dynamics change domestically and globally. It would also upend market planning along with agreements with payers, wholesalers, distributors and pharmacies.

The lack of an established acceptable price will make operating in Canada much more challenging and discourage research and commercialization of new medicines, ultimately harming patients and Canada's innovative ecosystem.

3. Examining the proposed investigation criteria

As a matter of principle, RAREi believes that it is inappropriate for the PMPRB to require patentees to set all "new" product prices at or below the median of the PMPRB11 to avoid an investigation. The term "excessive" implies an amount or degree that is too great to be reasonable or acceptable.

The PMPRB has acknowledged that the draft guidelines are a "paradigm shift," mainly in its strict adherence to the factors set out in s. 85 of the *Patent Act*. The PMPRB would abandon its traditional review of therapeutic value, and apply the same criteria to all products, regardless of the level of innovation they represent for Canadians and the health system. The PMPRB has failed to consult with health system stakeholders regarding this significant departure from current practice. While many medicines for rare disorders are first-in-class therapies and were already benchmarked against the median of the comparator countries (given the lack of domestic comparators), RAREi members also innovate in developing and commercializing new products for existing classes of medicines. The previous system while problematic, was at least predictable and provided some incentives to market a range of new medicines in Canada.

Furthermore, RAREi is very concerned with the board's proposed reliance on a domestic therapeutic class comparison (dTCC) as a primary factor in determining whether an investigation

could be pursued. While the existing price review system relies on the dTCC, it also provides for an assessment of therapeutic improvement which ultimately allows additional headroom above and beyond the dTCC. For example, if a product is deemed a substantial Improvement, it is permitted to set a price that is the higher of the median international price or the dTCC. Under the proposed regime, the allowable price would be limited to the lower of the median or dTCC regardless of level of innovation. In RAREi's view, the dTCC should only be used as a back-up in cases where no international prices are available within the PMPRB11, and comparisons should not include generics, biosimilars or non-prescription or non-approved treatments within the class. Comparing new innovative products to a class that includes such products undermines any incentives to research and launch new medicines in an existing class of products.

Some recognition of innovation is sorely needed. The suggestion that price comparisons would be made within a therapeutic class without any recognition of the numerous evolutions in treatment that emerge all the time is non-sensical. That would mean that allowable prices would not distinguish between modern, cutting edge treatments and older, often long-genericized medicines. By ignoring such improvements, and the clinical and quality-of-life improvements that arise from them, the board will undermine the innovation process and discourage medical progress.

It is also important to note that rare disease treatments are sometimes used without having been subject to randomized clinical trials focused on that particular disease given the small numbers of patients involved. However, clinicians rely upon these therapies because there are no other good options for patients. Comparators in such cases must be selected very carefully and attention should be given to ensuring that the new treatments are not being equated with out-dated, unsuitable or irrelevant alternatives.

Given that, RAREi requests that the PMPRB re-incorporate the concept of therapeutic improvement into its consideration of what constitutes a compliant price. RAREi would be pleased to engage with the board about how they might be operationalized.

In addition, RAREi disagrees with the board's proposal that the acceptable price for an "existing" medicine should be set at the highest price among the PMPRB11 because that approach will lead to the requirement for significant price adjustments for patented medicines that have remained compliant with the current guidelines, often for many years. It proposes instead that all "existing" products that were priced at or below the previously accepted NEAP prior to July 1, 2022 be deemed exempt from investigations. That approach will reward patentees for longstanding compliance and avoid substantial disruption in the patented medicines marketplace in Canada.

4. Implications of moving ahead with the proposed guidelines

As indicated above, the number of globally-launched medicines commercialized in Canada has declined every year since 2016, when the pricing reforms were initiated. In fact, since mid-2019,

more than half of all medicines approved in the US have not been submitted to Health Canada for approval.¹²

RAREi contends that the draft guidelines proposed by the board would exacerbate that already concerning trend by forcing prices of many innovative medicines down to unsustainable levels and by imposing a maximum price that fluctuates and is impossible to forecast. Rare disease, oncology, specialty, anti-bacterial, pandemic-related and chronic disease medicines will be particularly affected.¹³

Unfortunately, the board's proposed approach fails to provide clear and predictable rules for how companies can price their medicines in Canada. The maximum prices that companies can charge for their medicines will continuously fluctuate and the PMPRB staff will be given very broad discretion and powers for assessing prices. This unpredictability will make it extremely challenging to commercialize new medicines in this country and will deter many new medicines from coming to Canada.

That reality will also have some important knock-on effects, such as the ability of Canada to attract clinical trials and patient access to new innovations.

Assuming that innovators will look at conducting clinical trials in regions that will be among the primary launch wave countries, the new guidelines will result in fewer clinical trials taking place in Canada, which will in turn make it more challenging to retain and recruit physician specialists and physician researchers in this country. It will also have big financial implications for hospital, academic teaching institutions and research centres across Canada, which all rely heavily on innovator-sponsored clinical research to keep the doors open.

Similarly, a collective shift away from Canada by the innovative pharmaceutical industry's potential will add to an already challenging access environment for patients, particularly those living with rare diseases.

A March 2022 journal article reported that fewer than two-thirds of the rare disease treatments approved in Europe were submitted to Health Canada for regulatory approval, and among those approved by Health Canada, the rate of public reimbursement is low. Only 41 of the 63 rare disease medicines approved in Europe between 2015 and 2020 were submitted to Health Canada for review and only 32% achieved public reimbursement in Ontario, which was the highest percentage of products reimbursed among the Canadian provinces.¹⁴

Another comparative review, published in October 2021, examined public access to essential rare disease medicines in the US and Canada. It revealed that while Health Canada had approved

¹² Health Canada and US Food and Drugs Administration databases, last accessed November 4, 2022.

¹³ Research Etc., *Health Canada Pricing Reform research report*, January 21, 2021: <https://lifesciencesontario.ca/wp-content/uploads/2021/01/Impact-of-Health-Canada-Pricing-Reform-FINAL-Report-Jan-21-2021.pdf>.

¹⁴ Ward et al, *An international comparative analysis of public reimbursement of orphan drugs in Canadian provinces compared to European countries*. Orphanet Journal of Rare Diseases, Issue 17, Article 113, March 4, 2022): <https://doi.org/10.1186/s13023-022-02260-6>.

about 85% of the number approved in the US, on average only 54% of those were reimbursed by public drug plans in Canada.¹⁵

Together, these data demonstrate that rare disease patients, who are among the most disadvantaged members of our communities, will be further burdened if the PMPRB's proposed guidelines are implemented as presented.

As noted before, the PMPRB's proposed approach would also undermine the value of innovation and the market viability of new medicines. It would prevent Canada from building a stronger life sciences sector and health system, which has become a clear imperative for federal and provincial governments which are trying to get past the pandemic and deal effectively with strained health systems. As noted above, it will also have a negative impact on a number of other federal policy initiatives such as the proposed pan-Canadian genomics strategy, the evolving national rare disease treatment strategy and the life sciences and biomanufacturing strategy.

5. Concluding remarks

Rather than the onerous and regressive guidelines proposed by the PMPRB, which are inconsistent with the mandate articulated by the federal court, a more promising approach to regulating patented medicine prices would be to design a new price review regime from the ground up, working with stakeholders to ensure that it is fit for purpose and works within the Canadian health care system.

This is particularly important as Canadian payers – both governments and private insurers – are negotiating value-based and innovative agreements with rare disease developers. These agreements will not be possible where the medicine is not available for sale in Canada because there is no forecastable public list price, which has a huge impact on global commercialization prospects.

RAREi proposes a more progressive and collaborative approach that would position provincial health systems, patients and our vibrant medical research ecosystem for economic and health system recovery. It would also ultimately benefit the millions of Canadians affected by rare diseases, who rely on RAREi members to develop and deliver diagnostics and therapeutics to live and improve their quality of life.

¹⁵ Rawson, Nigel, *Availability and Accessibility of Essential Drugs for Rare Disorders in Canada*. Canadian Health Policy, October 13 2021: <https://doi.org/10.54194/HFEB4050> www.canadianhealthpolicy.com.