IMC Response to the PMPRB's 2024

Discussion Guide on the Board's Guidelines

September 11, 2024

Submitted via the PMPRB Website: https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/discussion-guide-phase2.html

This submission is made on behalf of Innovative Medicines Canada (IMC) in response to the July 2024 Discussion Guide, Phase 2, on the Board's Guidelines.[i]

IMC is the national association of biopharmaceutical and vaccine companies representing the majority of rights holders subject to the Patented Medicine Prices Review Board's (PMPRB) jurisdiction. The association advocates for policies that enable the discovery, development, and delivery of innovative medicines and vaccines to improve the lives of all Canadians and supports the members' commitment to being a valued partner in the Canadian healthcare system. Collectively, our sector supports more than 107,000 high-value jobs, invests upwards of $2.4 billion in R&D annually, and contributes nearly $16 billion to Canada's knowledge-based economy.

Background and context

IMC and its members believe that timely access to innovative medicines is a major Canadian public policy issue, given that patients have more limited, and significantly delayed access, to these treatments than patients in other G7 nations and in many OECD comparator nations.[ii] Delays to patient access in Canada has been identified among the top issues by the Council of the Federation under Ontario's leadership in 2024-25.Given their possible impact on launch dynamics, the PMPRB's Guidelines must be considered in this broader access and availability context and the full range of government pharmaceutical policies and priorities As previously highlighted, access and availability will be enhanced and supported by a clear and appropriately limited excessive pricing regime.

IMC has ongoing high-level concerns with the direction proposed in the Guidelines Discussion Guide. Prior to 2017, the PMPRB's practice was to encourage a high voluntary compliance through predictable benchmarks at the time of a medicine's launch. This appears to have been abandoned in favour of a more open-ended regime where PMPRB Staff will directly weigh the possible relevance of different excessive price factors in different product scenarios. This is particularly relevant for annual reviews and "in-depth" reviews where rights holders may not be able to determine an allowable price at the time of product launch nor throughout the product life cycle.

If pricing policies are adopted such as the median of the international price comparison, and therapeutic class comparisons conducted well after the time of product launch, the PMPRB will be operating beyond its mandate regarding patent abuse.[iii] It is also concerning that the PMPRB now proposes to determine allowable price through annual reviews using factors (e.g., international price points; annual reviews that would trigger in-depth reviews with evolving therapeutic comparators) that may be different than those which existed when a rights holder made its investment decision.

A major concern for rights holders is the unnecessary complexity, variability and discretion inherent in the options presented. The Discussion Guide contains elaborate and unclear process charts and proposes a complex review protocol (e.g., initial review, post-initial review, in-depth review, special provisions, and therapeutic class and similarity review). In IMC's view, PMPRB should validate if a patented medicine is priced non-excessively at introduction (i.e., at or below the highest international price (HIP) of the PMPRB11 schedule) and then monitor compliance with that introductory price, plus consumer price index (CPI) over time (referred to as the 'HIP policy' hereafter). Unnecessary complexity, variability, and discretion will cause compliance challenges for rights holders, who have historically been highly compliant with PMPRB's Guidelines, and will also reduce regulatory transparency for all interested parties.[iv]

IMC's responses on the specific Discussion Guide topics are set out below for the Board's consideration.

Consistency with an excessive price standard (Topic 1 – Price point)

As noted in IMC's previous submission, the median price point identified in the September 2023 amended Interim Guidance was adopted without reference to the PMPRB's mandate regarding excessive prices and detecting specific instances of patent abuse. IMC maintains that the MIP is inappropriate as a future mandated standard in conjunction with the revised schedule of international reference countries,[v] while the HIP is consistent with an excessive pricing standard.[vi]

The PMPRB has a newly created possible "midpoint" test in the 2024 Guidelines Discussion Guide, which may have been intended as a compromise between various party perspectives on their preferred price tests. However, the midpoint suffers from the same challenge as the median and serves to illustrate the arbitrary nature of selecting random price points below the HIP.

While the HIP is rooted in an excessive pricing standard, the median or the "midpoint" are consistent with pricing control. The jurisdictional basis or rationale for the latter two tests is unclear. Preference for a given price point is not a substitute for a policy rationale rooted in the PMPRB's mandate as interpreted by recent jurisprudence. As such, our position on Topic 1 remains that the PMPRB must adopt the HIP (Option 2).

Predictability precludes price re-benchmarking

As previously discussed, predictability over time is among the most important issues in the current Guidelines discussion for rights holders.[vii] Re-benchmarking is foreseeable through the proposed annual price reviews and in-depth reviews. This would effectively create arbitrary price reductions (see PMPRB's analysis of price reviews during Product Life cycle 2023 Scoping document, Box 3, Pricing trends in Canada versus the PMPRB11). Based on this data, re-benchmarking would clearly reflect price control over time, which is inconsistent with an excessive pricing mandate.

Rights holders need and expect a predictable maximum non-excessive price over the life of a product, subject to potential CPI adjustments. The PMPRB could still routinely monitor and validate compliance with the CPI-adjusted price benchmark established at a medicine's introduction without re-benchmarking prices on an annual basis. A requirement that the ceiling price of a patented medicine decrease over time on an annual basis, or other time-based reduction processes, are inconsistent with preventing patent abuse.[viii]

Full exemption for existing products is required (Topic 2)

IMC has consistently positioned that a full exemption for existing products is required. Existing products were already compliant and therefore non-excessive with the applicable legislation and Guidelines, given that the amended Regulations did not change the excessive price factors under the *Patent Act*. The PMPRB had previously provided a transition measure for existing products whereby existing products could receive the HIP of the revised PMPRB11 basket.[ix] If the PMPRB implements the HIP standard, in accordance with its mandate, it may reduce issues for some existing products. As previously discussed, the PMPRB could alternatively anchor a transition policy to the Consumer Price Index (CPI) provisions of the *Patent Act*.[x]

Regardless of pricing policy, Option 3 setting out a three-year transition would be more appropriate for the Canadian pharmaceutical supply chain, which is already struggling due to a variety of cost control policies. Rights holders and other supply chain participants (e.g., pharmacists, distributors, pharmacies and generic manufacturers) were created and executed on business plans based upon the previous regime and should not be penalized for the ongoing uncertainty with respect to the new Guidelines. [xi]

Consumer Price Index (CPI) methodology (Topic 3)

The PMPRB has a long-standing CPI methodology. In implementing the HIP policy noted above, the existing CPI methodology can be used to adjust the ceiling over time. IMC and its member companies have many questions about the nature of the annual price reviews noted in the Discussion Guide and how they relate to CPI. IMC submitted a number of questions to the PMPRB which were not addressed during the August 13th 2024 webinar. As such, it is difficult to comment upon specific details such as CPI calculation, given that key aspects of a new regime, such as the functional role of annual price reviews, remain unknown.

CPI is specifically referenced in the *Patent Act*, and the PMPRB's Guidelines clearly acknowledge the allowability of CPI adjustments as permitted under the statute. Until the fundamental role of CPI within the regime is clarified, and as a practical matter, the PMPRB must continue to update and post its *CPI-Based Price-Adjustment Factors for Patented Drug Products* on an ongoing basis. Further comparison of this existing CPI methodology and the proposed new CPI calculation in the Discussion Guide, and rationale for changes, should be a subject for further discussion as part of a technical working group consisting of rights holders and PMPRB staff.

Complaints and eligibility (Topic 4)

IMC maintains that the most effective excessive price review system would consist of transparent and predictable Guidelines that provide price tests for the patented medicines under its jurisdiction. In general, the PMPRB should focus more on the substance of complaints and how to resolve them. If a price appears to exceed the ceiling set out by the price tests, then an investigation could be undertaken to determine if the test was appropriately applied in the circumstances. Under a HIP policy, complaints could be easily resolved with a check against the HIP.

In general, eligibility for complaints should be narrow, transparent, consistent with s. 86(2) of the *Patent Act,* and restricted to the Federal Minister of Health or any of his/her Provincial or Territorial counterparts (i.e., Option 1 is most appropriate).

As discussed below, IMC has more fundamental issues with the in-depth review process and therefore encourages additional technical dialogue with rights holders to identify a path forward.

Complaints-only processes (Topic 5)

The topic of vaccines being considered under a complaints-only based process should now be a settled matter. [xii] As previously iterated, IMC is in favour of all tendered products (including vaccines and blood products) being considered in this manner. In general, a HIP Policy would reduce the need for in-depth reviews, complaints-based carve outs, and would help to address other regime efficiency issues.

In-Depth reviews (Topic 6)

The questions and options under Topics 4, 5 and 6 of the Discussion Guide are insufficient for interested parties to provide the PMPRB with appropriate input to address the many ongoing issues and concerns with in-depth reviews (please see the attached appendix of IMC member questions). Subject to the adoption of an appropriate price test, in-depth reviews are considered by rights holders as the main Guideline policy that they must account for when making pricing and launch decisions. Under the current proposals, there is no way for a rights holder to predict the outcome of an in-depth review, and this absence of clarity may impact corporate decisions regarding the introduction of new medicines in Canada.

Previous proposals for a domestic therapeutic class comparison (dTCC) included inappropriate comparisons to generic medicines, unpredictable reassessments of the dTCC over time, 'lower-of' tests, and would have driven prices below non-excessive pricing standards based on international referencing. Such proposals remain problematic and should be avoided.

The *Patent Act* does not require the PMPRB to conduct a detailed examination of clinical performance nor a consideration of comparators as identified by Health Technology Assessment (HTA) per the Discussion Guide.[xiii] Pharmacoeconomic value was ruled to be an unconstitutional price determination factor[xiv]. It is therefore both surprising and concerning that the usage of HTA to determine the relevance of clinical comparators is referenced in the Discussion Guide, and we suggest this be removed.

The proposal for PMPRB staff to conduct a detailed relevance assessment also requires careful consideration. We are not in a position to offer a response to either topic 6, Option 1: "one level of similarity is identified for the comparators as a whole" (general comparability assessment) or Option 2: "each comparator will be assigned a level of similarity" (granular comparability assessment) because the fundamental role of such a comparability assessment is unclear. IMC does not understand how the PMPRB would use these comparators, criteria for comparator selection, and weightings against more concrete and objective factors such as pricing in the PMPRB11 countries. Companies and HTA bodies do not always agree on appropriate comparators nor the degree of similarity of products in the same therapeutic class. Perceived degrees of comparator similarity are not an objective basis for weighing one *Patent Act* factor against another.

A key challenge with the in-depth review is the broad discretion that PMPRB staff would be afforded to identify comparator relevance, and weigh *Patent Act* factors on a case-by-case basis (section 5.4 In- Depth review – "Prices will

be identified for the comparators and Staff will consider the relevance of the comparators… Staff will then consider the strength of the therapeutic comparators, the relevant IPC, and the CPI on a case-by-case basis).

PMPRB staff may not have the clinical expertise to consider and weigh relevance of comparators, nor have criteria to establish relevance been appropriately specified for them to do so.

In-depth reviews have not been sufficiently articulated in the Discussion Guide. IMC suggests fundamentally reconsidering the purpose and practicality of these proposals. Technical working groups with experts representing rights holders should be created to identify a path forward.

Future role of HDAP – (Topic 7)

It is premature to comment on timing and nature of scientific reviews, and the future role of the Human Drug Advisory Panel (HDAP), without additional information on the future Guidelines envisioned by the PMPRB and how scientific review and comparator weighting may or may not relate to the determination of an excessive price.

Other parameters around investigations will depend on the nature and complexity of the Guidelines proposed by the PMPRB. This and other ideas around file dispute resolution mechanisms should also be discussed further through a technical working group.

Common sense file resolution mechanisms needed

The PMPRB should ensure that year-to-year changes and/or methodological considerations such as exchange rate fluctuations (notably but not exclusively) do not produce unnecessary regulatory burden for all parties negatively impacting the cost of marketing drugs in Canada.

The draft Guidelines should include some reasonable buffers or tolerance factors (e.g. +/- 5 to 10% fluctuation against the PMPRB11 benchmark) to ensure changes in exchange rates do not result in unnecessary regulatory burden when domestic prices are otherwise stable. This is similar to previously proposed measures. This and other possible common sense file resolution mechanisms[xv] would be particularly helpful for smaller biotech companies who often do not have the support of large and specialized teams to manage PMPRB pricing dynamics (e.g. four decimal place precision).[xvi]

Guidelines next steps

IMC commends the PMPRB for not advancing the Fall 2022 Guidelines Proposals, which were fundamentally flawed. We also appreciated the effort to develop case studies in the context of this consultation. However, the case studies raise new concerns that the PMPRB envisions a high degree of case-by-case management and context-specific weighing of factors, which would be inappropriate and unnecessary in light of its mandate.[xvii]

IMC remains disappointed that we have not been able to engage with the PMPRB in a more iterative manner including through technical working group(s). We again request direct dialogue with the PMPRB during its Guidelines consultation process, which is consistent with previous successful practices (e.g. the collaborative DIP methodology technical working group discussions).

As a final comment, IMC notes that during the 2023 consultation with rights holders and other interested parties, it was suggested that the PMPRB could assist with ongoing access challenges in Canada by providing faster initial assessments. While such efficiencies may be desirable, the main issues for rights holders with the new PMPRB Guidelines are alignment with the Board's statutory mandate, and ensuring that the new system provides stability and predictability while medicines are under the Board's jurisdiction. By addressing the two aforementioned issues, the PMPRB will be doing its part to improve availability and access to new medicines in Canada.

Thank you for your consideration of our submission.

Appendix – Questions from Rights holders (non-exhaustive)

The following questions were not addressed during the August 13, 2024 webinar.

International price referencing

- Will annual price reviews result in price ceilings that become lower over time? If so, how is this consistent with the PMPRB's excessive price mandate?
- What PMPRB action would an annual price review specifically trigger in the event that an international price benchmark has changed year-over-year?
- Will draft Guidelines include reasonable buffers (e.g. +/- 5-10% fluctuation) to ensure minor year-to-year changes and/or methodological considerations (e.g. exchange rate fluctuations) do not result in unnecessary regulatory burden (e.g. when prices are generally stable)?
- What is the rationale for possible price tests below the highest international price of the PMPRB11 schedule?
- How will the PMPRB treat medicines that are available in Canada but never available in any other PMPRB 11 country?
- What are the measures to encourage companies to view Canada as a viable first international launch market?
- Will a predictable exchange rate policy be published as part of an updated Guideline?
- How will Initial Price Reviews be done for new formats/strengths of an existing medicine? Would these be assessed similarly to international prices of the same strength?
- Will flat pricing be permitted for new strengths and formats?
- When will a non-excessive price be determined (e.g., after how many PMPRB11 countries launch and/or # of years)?
- If a medicine passes the IPC test during the initial and post-initial price review, would it be considered "within guidelines"?
- In what cases would an international price comparison not suffice? Could you please identify specific situations that would require an in-depth review?

Therapeutic price referencing

- What is the rationale for possibly employing Health Technology Assessment for the selection of comparators given that the previous pharmacoeconomic value factor was deemed unconstitutional?
- What medical or scientific qualifications would those responsible for determining relevant therapeutic comparators have?
- Is first sale a reference point for the conduct of TCC? Or would TCC use clinical/pricing information available at the time of an in-depth review? Will PMPRB Staff consider comparators introduced after the launch of the new medicine to be appropriate for the conduct of TCC?
- How would comparators be selected? What would be the sources for comparator selection?

- How would comparators be weighed (or their relevance determined)? How would level of similarity be defined?
- Which indication would be considered in the TCC test? Would comparators be limited to those available during the introductory period?
- How would PMPRB ensure consistency and procedural fairness in complex reviews and specifically comparator selection?
- How will the PMPRB ensure transparency and predictability in the in-depth review process when there seems to be significant discretion for staff and limited information on methodology and tests used to determine non-excessiveness?
- How would clinical experts and patients be involved in the comparator selection process?
- How would disputes between manufacturers and PMPRB staff regarding comparator selection be addressed?
- Would in-depth reviews be made public? – PMPRB August 13 webinar suggested no. Please confirm.
- How would PMPRB incorporate rights holder perspectives and expertise for in-depth reviews?
- Would the top of the domestic therapeutic class comparison be used?
- If a product has more than one indication at time of in-depth review, which indication will be evaluated – and how will this indication be confirmed?
- How will in-depth review be conducted for a medication without comparators (dTCC/iTCC)?

Consumer price index

- How will international price reviews that may decrease over time be balanced against the Patent Act's CPI factor?
- Will consumer price index be factored into the price ceiling for every patented product?

Process and reporting

- Will PMPRB issue compliance reports or comparable documents?
- What efforts is PMPRB taking to reduce regulatory burden for all medicines?
- Will Voluntary Undertakings be published?
- Will the historical information on hearings, VCUs and PMPRB compliance be restored on the PMPRB website?
- What information will be included in semi-annual status reports?
- Would rights holders be invited to make submissions regarding the TCC prior to the commencement of in-depth reviews?
- How would Post-Initial Reviews be handled after a product goes through its first In-depth Review? If an In-depth Review is closed with no further action, would the medicine's threshold for triggering another In-depth Review be adjusted?
- Would an In-depth Review assess the list price of the medicine based on its first indication, or all indications that have been approved by Health Canada at the time of In-depth Review?
- Would all complaints automatically lead to In-depth Reviews, or would there be a step before to assess whether the complaint is valid?
- What criteria would be used to establish the validity of a complaint?
- Will the PMPRB make public the person or party that files a complaint? Will there be a filtering system for complaints?

Transition

- Why did PMPRB remove grandfathering provisions that were previously identified?
- How will products launched before July 1, 2022 but without a NEAP be assessed?
- Under Section D, In-Depth Review:
    - Why does the PMPRB believe that "Most medicines are not subject to further action" What is this based upon?

- What happens to a medicine with a MAPP and NEAP, but presently no IPC is possible (lack of public prices across PMPRB11)? Will this trigger in-depth review?
- If the definition of new medicines does not allow for a transition period for medicines launched but without a NEAP as of July 1, 2022, would such medicines be considered for an in-depth review immediately upon the coming into force of the Guidelines? The lack of transition period means that "new medicines" could be considered excessive overnight just by virtue of the July 1, 2022 coming into force.

Other

- How will combination products be assessed?
- Will products addressing antimicrobial resistance be subject to therapeutic referencing?
- How will PMPRB achieve transparency and predictability around the balancing of factors identified on page 15?: "The balancing of the factors is not defined by legislation or regulation. As in the past, when crafting recommendations to the Chairperson, Staff will set out how the balancing is affected by the available evidence, and its recommended weight, which can vary on a case-by-case basis (see section 8 for case study examples), while also ensuring that it is applying its balancing methodology consistently to ensure fairness between all Rights Holders."
- What is the escalation process if PMPRB does not meet communicated review timelines (i.e. 60 days). And what are the key performance indicators for response to manufacturer's questions?
- When can products deemed "under review" during the period of interim guidance expect to have their reviews under the new guidelines completed?

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[i] IMC understands that the PMPRB intends to issue Guidelines following amendments to the Patented Medicines Regulations (Regulations) which came into force July 1, 2022. While IMC is committed to constructive engagement with the PMPRB on the Guidelines, IMC's engagement is not intended and should not be interpreted as supporting the amendments to the Regulations, the August 2022 interim approach, the September 2023 amended interim approach, or the final Guidelines. IMC reserves the right to oppose any aspect of the amended Regulations, Guidance, or Guidelines that exceed the jurisdiction of the Board. There are a number of Guidelines-related issues that had been identified in previous IMC submissions that have not yet been addressed and which require future consultation (please see IMC's February 2020, August 2020, February 2021, August 2021, July 2022, December 2022, August 2023, and December 2023 submissions).

[ii] This is due to many factors, including without limitation regulatory inefficiencies and duplication, narrow and inflexible Health Technology Assessment (HTA) recommendations, and the application of processes designed for conventional pharmaceutical products to complex new technologies.

[iii] e.g., *Merck c Canada,* 2022 QCCA 240 *and Alexion v Canada,* 2021 FCA 157.

[iv] Monitoring prices over time does not require or enable the PMPRB to force prices downward over time.

[v] In IMC's view, this is inconsistent with an excessive price standard, and recent appellate court decisions that have delineated the role of the PMPRB within its constitutional and legislative limits. Rights holders should be considered compliant with the new basket provided their submitted Canadian prices are within the range of available prices of the revised PMPRB11 schedule. The government has already removed the two higher-priced countries (Switzerland and the United States) from the international schedule, which has the effect of constraining the ceiling price of New Medicines. The PMPRB should not further constrain prices by selecting the median as a reference point in future Guidelines.

[vi] Prices above that level may be justifiable in some circumstances and rights holders should be afforded an opportunity to substantiate prices with the PMPRB.

[vii] There has been considerable feedback from rights holders and other interested parties that any form of re-benchmarking (either through application of the international schedule, or therapeutic referencing) would pose significant predictability concerns. The PMPRB has functioned for decades without re- benchmarking and provincial product listing agreements and private payer agreements effectively control pricing over time. The PMPRB can address predictability concerns by including a

statement in the Guidelines that "once a product is determined to be 'compliant' or 'reviewed,' the PMPRB will not reassess or 're-benchmark' the product, provided the rights holder does not increase its price by more than CPI."

[viii] A product should be considered compliant over time provided it does not exceed its at-launch price (plus Consumer Price Index adjustments).

[ix] The draft 2022 guidelines had investigation criteria for Existing Medicines based on the lower of: (i) existing NEAP, and (ii) HIP PMPRB11. See 2022 backgrounder p. 4

[x] From a practical perspective, existing products could be determined as non-excessive going forward, provided their national average transaction price (N-ATP) does not exceed the most recent non-excessive average price (NEAP), as adjusted by the CPI for 2023, 2024 and onwards. Or other measures to ensure that products first sold prior to the amended regulations coming into force are reviewed against the PMPRB7 international schedule (e.g. those first sold before July 1, 2022, but that do not yet have a NEAP).

[xi] It is also important to note that some rights holders launched patented medicines "at risk" (in absence of final PMPRB Guidelines) following the enactment of revised Regulations on July 1, 2022. In the event of issues arising from the lack of final Guidelines, these products could be gradually transitioned to the Highest International Price (HIP) of the PMPRB11, or alternatively, rights holders could be afforded the opportunity to substantiate prices directly with the PMPRB. IMC takes this opportunity to reiterate the PMPRB's commitment that "once new Guidelines are in place, no potential excess revenues will be calculated by staff retrospectively for any New Medicines for sales made during the interim period." https://www.canada.ca/en/patented-medicine-prices-review/services/legislation/interim-guidance.html

[xii] "88. Notwithstanding the above, in the case of Biosimilars, medicines for veterinary use, over the counter (OTC) medicines, and vaccines, an investigation will only be commenced by Staff if a complaint is received." https://www.canada.ca/content/dam/pmprb-cepmb/documents/legislation/guidelines/PMPRB-Guidelines-en.pdf

[xiii] "The approach for defining a level of similarity would evaluate clinical evidence such as efficacy, safety, adverse event profile, route of administration, and patient convenience, among other possible considerations. Evidence would be considered based on recognized standards of quality, with information from high-quality peer-reviewed publications, including phase III head-to-head clinical trials, high-quality networked meta-analysis or **health technology assessment** given the greatest weight" [emphasis added].

[xiv] *Merck c Canada*, 2022 QCCA 240,

[xv] For example, new manufacturers considering Canada and start ups have commented on the need to understand their price prior to making enormous investment into infrastructure and have suggested a process to discuss or pre-confirm compliant pricing that manufacturers could opt into.

[xvi] Small companies have noted the challenges of holding a manufacturer to potentially significant exchange rate fluctuations that are outside of their (and Canada's) control and that this may impact the sequence of Canada in global launches and Canada as a viable, predictable market.

[xvii] More intricate and nuanced case studies than those presented will be needed and should be discussed through technical working groups.