BIOTECanada Response to
'Shaping the Future: A Discussion Guide for PMPRB
Phase 2 Consultations on New Guidelines'

September 11th, 2024

BIOTECanada is providing written feedback on the PMPRB's **Shaping the Future: A Discussion Guide for PMPRB Phase 2 Consultations on New Guidelines** ("the Discussion Guide") published on June 26, 2024.

BIOTECanada consists of more than 240 members, primarily patentees, that are dedicated to bringing life changing therapies to Canadian patients. Our association's membership is representative of the Canadian biotechnology ecosystem, including emerging research-focused small and medium sized enterprises, universities, investors, incubator, and accelerator organizations, as well as multi-national companies. Our members are at the forefront of producing the next generation of health care solutions and biologic based medicines, including vaccines, therapies for rare diseases, cell and gene therapies, and many new dynamic technologies holding great promise for the future of healthcare.

The Canadian biopharmaceutical ecosystem has changed significantly since the PMPRB's 2010 Guidelines were instituted. The biotechnology industry has achieved significant advancements in numerous therapeutic areas such that previously untreated conditions now have the possibility of a cure. Canadian pricing and reimbursement institutions, including Canada's Drug Agency (CDA-AMC), l'Institut National d'Excellence en Santé et Services Sociaux (INESSS), and the pan-Canadian Pharmaceutical Alliance (pCPA), each with mandates distinct from the PMPRB and existing mechanisms to assess the value of medicines, have evolved to reflect this changing ecosystem.

The PMPRB as a quasi-judicial body must operate at arms-length from these other players, and the updated Guidelines should reflect PMPRB's defined role in the biopharmaceutical ecosystem, which is to ensure that rights-holders do no abuse their patents by charging an excessive price – the upper limit under which all other stakeholders are highly capable and well positioned to freely operate in the various markets for reimbursing and funding drug technologies in Canada. BIOTECanada welcomes the PMPRB's acknowledgement that "transparent, predictable, and procedurally fair Guidelines provide an efficient way for rights-holders to manage risk"[1]; indeed, it is essential the PMPRB ensures that future Guidelines support a stable pricing environment and provide predictability for rights-holders, as they will inform rights-holders' decision-making years in advance of a launch of a new medication.

[1] Shaping the Future: A Discussion Guide for PMPRB Phase 2 Consultations on New Guidelines - Canada.ca

BIOTECanada's key asks to the PMPRB related to the Discussion Guide include:

- Implement the Highest International Price (HIP) as the only appropriate mechanism at introduction to triage for potential excessive pricing; HIP is aligned with PMPRB's legislative mandate.
- The prices of Existing Medicines must not be subject to additional price review in the new Guidelines.
- BIOTECanada requests the PMPRB maintain lagged CPI methodology for consistency and efficiency.
- The current proposal around In-Depth Reviews does not provide enough clarity and predictability to support rights-holders in their pricing decision; the details surrounding the implementation of an In-Depth Review must be shared in the proposed new Guidelines.
- Complaints that trigger an In-Depth Review must be transparent, substantive, and fall within the mandate and decision-making authority of the PMPRB. BIOTECanada requests the PMPRB to convene a Working Group to clearly define criteria for complaints.
- All vaccines should be regulated in a complaint-based manner.
- Given PMPRB's excessive pricing mandate, use of the highest/top of TCC is the only appropriate way to apply the TCC, and a medicine should receive the higher of TCC or HIP+CPI. BIOTECanada requests the PMPRB to convene a Working Group on the TCC.
- HDAP should be an independent body with clearly defined guidelines to act as an impartial advisor to the PMPRB process. BIOTECanada requests the PMPRB to convene a Working Group to determine the future role and mandate of HDAP.

More detail is provided in the responses to each topic below.

Topic 1: Price level within the PMPRB11 to be used in the initial and post-initial price review:

Option 1: MIP Option 2: HIP Option 3: midpoint between the MIP and HIP

The only appropriate price level within the PMPRB 11 to be used in the initial and post-initial price review is the Highest International Price (HIP) comparison i.e. Option 2. Canadian ex-factory prices that do not exceed the PMPRB11 countries, all of whom have some form of price regulation in place, are not excessively priced by definition and thus should not be seen as priorities for investigations. HIP is aligned with PMPRB's legislative mandate, as defined in the *Alexion*[2] and *Merck* (Quebec Court of Appeal) decisions[3]; any threshold lower than HIP would be outside of the jurisdiction of the PMPRB. Use of the HIP of the new PMPRB11 basket of countries would already significantly constrain prices (based on the removal of the US and Switzerland, and the addition of typically lower-price countries).

Because the PMPRB11 basket is composed entirely of countries that regulate medicine prices, it follows that none of the PMPRB11 prices can plausibly be considered "excessive." After introduction, CPI-based increases to list prices should not trigger investigations. Once the ceiling price of a medicine is established at its introduction to the Canadian market, PMPRB staff should not "re-benchmark" (i.e., reassess) the ceiling price over time for any reason other than allowable inflation-based adjustments. This approach provides the predictability and stability the sector requires to invest in new technologies that have very long discovery and development timelines. It also aligns with PMPRB's stated objectives, which are to enhance the Board's administrative efficiency, and to provide transparency and predictability to Rights-holders.

[2] Alexion Pharmaceuticals Inc. v. Canada (Attorney General) - Federal Court of Appeal (fca-caf.gc.ca)
[3] *Merck v. Canada (AG)*, 2022 QCCA 240, par. 143-146.

The Median International Price (MIP) (Option 1) and the midpoint between the MIP and the HIP (Option 3) are not appropriate for this purpose for a number of reasons. Only the HIP defines an upper limit while the use of the MIP or the midpoint of the MIP and HIP as price limits would be arbitrary as their selection would not be based on any generally-accepted definitions of excessiveness; arbitrary selection of a price threshold is the same as implementing a price control measure.

Additionally, the use of the MIP or the midpoint between the MIP and HIP does not align with the Guidelines' purpose of providing clarity and certainty for rights-holders to support their pricing decision as these arbitrary price points are potentially subject to considerable changes due to foreign exchange fluctuations. Finally, Options 1 and 3 would impact administrative efficiency - approximately 78% of all DINs would be subject to an In-Depth Review if IPC is set to the MIP, and approximately 53% if IPC is set at the midpoint between the MIP and HIP.

Introductory pricing assessment should not be performed until a minimum of five countries, or three years have passed. This enables Canada to be in the first wave of launches, bringing innovative medicines to patients quickly. If the introductory price test is done on two countries at launch, the manufacturer may delay the launch in Canada until a higher (or highest) price country launches. BIOTECanada does not support having an interim price.

Topic 2: The length of time Staff should wait, following the implementation of the Guidelines, to determine whether the IPC identification criterion for an Existing medicine is met:

Option 1: one year *Option 2: two years* *Option 3: three years*

BIOTECanada does not support any of the three options proposed by the PMPRB as the prices of Existing Medicines must not be subject to additional price review in the new Guidelines. The approach for existing products (previously referred to as 'grandfathering') should be as follows: medicines and their line extensions sold at non-excessive prices prior to implementation of the new Guidelines, with the addition of allowable CPI, should be presumed to be non-excessive moving forward. This is consistent with the existing products provisions when the Guidelines were last revised in 2010.

This approach for existing products ensures crucial predictability to both existing patentees and to stakeholders more broadly (including wholesalers, distributors, pharmacies and others in the supply chain). Patentees set these prices, in part, to comply with Guidelines in effect at the time, and then entered into reimbursement, distribution, and dispensing agreements based upon those prices. Patentees and the other stakeholders had a reasonable expectation that these prices would, for the most part, remain non-excessive in the future. As the 2023 Scoping Paper noted, 76% of existing medicines, which were deemed compliant under the PMPRB7 and 2010 Guidelines, are currently priced above the MIP. Forcing price reductions to these products, which represent 85% of patented medicine sales, by changing reference countries would be a significant disruption to stakeholders and may be considered a form of price control beyond the PMPRB's mandate.

Moreover, reconsidering the prices of Existing Medicines would create substantial administrative burden. According to PMPRB CIMS 2022 and 2023, 768 patented DINs are from an existing medicine and would be subject to reassessment. Depending on the IPC chosen in the final guideline, a minimum of 61% or 265 patented DINs (if HIP is chosen) up to 82% or 633 patented DINs (if MIP is chosen) of existing medicines would be subject to an In-Depth Review, all of which have previously undergone review at the time of their launch by PMPRB and were deemed non-excessive.

Topic 3: In-Depth Review based on CPI increase criteria:

- *Option 1: if the list price increase is above one-year CPI*
- *Option 2: if the cumulative increase in list price over the last two years is above the combined CPI for the past two years and the increase only took place within the last year (i.e. no increase in price in the first of the two years, followed by an increase on the second year)*

BIOTECanada recommends Option 2. Post-initial review should be based on CPI exclusively (and not an IPC) and after introduction, CPI-based increases to list prices should not trigger In-Depth Reviews. Moreover, once an initial review has been conducted following introduction, it should not be subject to re-benchmarking over time via a process of Annual Price Review. This approach provides the predictability and stability the sector requires to invest in new technologies that have very long discovery and development timelines.

Price adjustment based on CPI is critical to allow companies to adapt their pricing changes according to Canadian economic conditions. The CPI adjustment methodology from PMPRB was last amended and implemented in 2015 to adopt Actual Lagged CPI methodology in order to "reduce the regulatory burden on patentees and to make effective use of Board Staff resources without adversely affecting the PMPRB mandate to protect consumers."[4] BIOTECanada requests the PMPRB to maintain lagged CPI methodology for consistency and efficiency in processes.

Topic 4: The individuals/groups permitted to submit a complaint:

- *Option 1: limit complaints to the Federal Minister of Health or any of his/her Provincial or Territorial counterparts*
- *Option 2A: limit complaints to option 1 above plus public payors only; or*
- *Option 2B: limit complaints to option 1 above plus private and public payors*
- *Option 3: limit complaints to everyone except for Rights-holders.*
- *Option 4: no limits/restrictions.*

BIOTECanada supports a streamlined and transparent complaints system: complaints should be limited to the Federal Minister of Health or any of his/her Provincial or Territorial counterparts i.e. Option 1. Those who wish to submit a valid complaint may do so through one of these channels, and should be identified to the patentee. If not delimited, the proposed complaints system could become unmanageable and/or subject to abuse, hampering critically-needed predictability for rights-holders.

Complaints that trigger an In-Depth Review must be substantive and fall within the mandate and decision-making authority of the PMPRB (i.e. issues of excessive pricing and patent abuse). We would recommend establishing a Working Group to define criteria for complaints in an open and transparent manner.

[4] New Lagged CPI-Adjustment Methodology Initiative – 2015 Implementation (pmprb-cepmb.gc.ca)

Topic 5: Expanding the list of products that would only be subject to an In-Depth Review following a complaint to include biosimilars and/or vaccines.

- *Option 1: The PMPRB will treat patented biosimilars and/or vaccines the same as other medicines.*
- *Option 2: The PMPRB will only open an In-Depth Review for biosimilars and/or vaccines when a complaint is received.*

The PMPRB should focus its attention on medicines for which patent abuse is possible. Medicines with patents that cannot be abused due to factors such as competition or specialized Canadian purchasing processes should be subject to In-Depth Reviews only when a complaint is received within a fair and transparent complaint system where the complaint aligns with a pre-specified definition of an acceptable complaint. Thus, BIOTECanada recommends Option 2, with some additions. Medicines that should only be subject to an In-Depth Review following a complaint include:

- Vaccines
- Biosimilars
- Patented medicines that have lost exclusivity and are multi-source (i.e., biosimilar or generic competition exists)
- All medicines procured exclusively through government contracts and tenders (e.g., Canadian Blood Services / Héma-Quebec)

Spotlight on Vaccines

BIOTECanada is requesting that all vaccines be regulated like generic and veterinary medicines, in a complaint-based manner, where they only need to file pricing and other information to the PMPRB if specifically asked. We recommend a collaborative relationship between the industry and government to finalize new PMPRB Guidelines through meaningful consultation.

The Canadian market for vaccines already has unique measures to ensure competitive pricing and security of supply. These include strict Health Canada reviews, evaluations by the National Advisory Committee on Immunization (NACI) and the Canadian Immunization Committee (CIC), and multiple procurement processes. Vaccine prices in Canada cannot exceed those in the PMPRB11 comparator countries.

During the consultation process, it is crucial to consider how changes to the Guidelines could affect vaccines, as their reimbursement process differs from that of pharmaceutical products. BIOTECanada believes that vaccines are a prime example of a class of patented products for which there is low risk, and therefore should be managed with limited regulatory burden including adoption of a “complaint” based approach.

Topic 6: Use of clinical evidence to contextualize the degree of similarity of comparators identified for the TCC.

- *Option 1: one level of similarity is identified for the comparators as a whole.*
- *Option 2: each comparator will be assigned a level of similarity.*

BIOTECanada recommends that the PMPRB establish a Working Group on this topic as there is insufficient information provided in the Discussion Guide to allow one to choose one of the two options or to propose an alternative. Moreover, the TCC (including both dTCC and iTCC) is a complex concept with special nuances that must be considered, including inherent variation, making this an ideal and critical candidate for a working group of technical experts drawn from rights-holders.

Use of the highest/top of the TCC is the only appropriate way to apply the TCC, and a medicine should receive the higher of the TCC or HIP+CPI in order to ensure that the PMPRB is operating within its constitutional mandate (these principles should apply in any approach to the TCC, since it is consistent with the PMPRB's legislative mandate to prevent excessive pricing). However, the discussion guide does not state this explicitly and lacks sufficient detail to understand how the TCC will work in practice.

Defining the operation of TCC in an In-Depth Review is required to meet the PMPRB's stated principles of transparency, fairness and predictability. More information is required on how comparators are going to be selected, and any new Guidelines must preserve the incentive for patentees to seek Health Canada authorization for new indications. It is important to note that price reductions triggered by a re-assessment in the middle of a product's lifecycle introduces significant unpredictability for patentees and complexity to the system. This will negatively impact a rights-holder's ability to launch new indications, provide comprehensive patient support and may interfere with industry's ability to sustain existing listing agreements. To achieve the Guidelines' purpose of providing clarity and predictability for rights-holders to use to support their pricing decisions, the specific details surrounding the implementation of an In-Depth Review must be published in the final guidelines. To reiterate, BIOTECanada recommends that this topic be explored through a technical working group.

Topic 7: Future role of HDAP

- *Option 1: HDAP will be used only on an ad hoc basis when deemed necessary by Staff.*
- *Option 2: No HDAP – the scientific process will be conducted by Staff.*

As described within the Discussion Guide, the role of HDAP in this new process (wherein levels of therapeutic improvement are no longer assessed) is unclear. BIOTECanada supports HDAP playing an independent advisory role to PMPRB Scientific Staff on an ad hoc basis, potentially as an avenue to provide meaningful input on the TCC (while maintaining that the ceiling should be the higher of HIP+CPI or TCC). However, new Guidelines should ensure fairness and consistency regarding when and how HDAP advice is employed by Staff.

Importantly, rights-holders and not just staff should have access to HDAP; specifically, an HDAP review should be part of an escalation pathway in cases where rights-holders and PMPRB Scientific Staff disagree. Additionally, Staff should have access to subject matter experts who can support and / or validate their assessments; These experts should be included when a rights-holder makes a request for reconsideration following the issuance of a Staff recommendation. The ability to have dialogue, transparency and a fair process is key to HDAP playing a meaningful and effective role.

HDAP should be guided by clear principles. The role and mandate of HDAP should be included in the Working Group requested above i.e. the recommended TCC Working Group.

Conclusion

BIOTECanada acknowledges the PMPRB's position that "transparent, predictable, and procedurally fair Guidelines provide an efficient way for rights-holders to manage risk"[5] and would welcome measures to ensure accountability in executing on these principles. Tools that are in place to measure the PMPRB's effectiveness should be updated to ensure alignment with the PMPRB's legislative mandate. For example, the PMPRB's Departmental Results Report uses the percentage of patented drug prices in Canada below the median of the PMPRB's comparator countries as a key performance metric, with the target being 50%.[6] In our view, this metric is not aligned with the PMPRB's mandate. In addition, the PMPRB should develop and share a financial assessment of the impact of the changes being proposed in the new Guidelines.

BIOTECanada strongly encourages the PMPRB to enhance communication and engagement with stakeholders via face-to-face meetings and technical working groups. It is through effective and transparent collaboration that durable Guidelines can be developed to provide patentees with the predictability and clarity needed for compliance and ensure a sustainable Canadian biotechnology ecosystem.

BIOTECanada requests that the PMPRB establish meaningful Working Groups when developing the new Guidelines. For example, the 2011 DIP Technical Working Group, which consisted of representative stakeholders and PMPRB Staff, provides an important model of an effective working group and should be emulated. Experienced members would be able to "stress-test" the Guidelines in a Working Group structure and help develop clear language to prevent ambiguity, contradiction, and unforeseen or counter-productive outcomes before the Guidelines are published.

BIOTECanada and its members appreciate the opportunity to provide feedback on the Discussion Guide. Collectively, we are eager to work cooperatively with the PMPRB to establish drug pricing policies that prioritize the health of Canadians and ensure a sustainable health care system.

[5] Shaping the Future: A Discussion Guide for PMPRB Phase 2 Consultations on New Guidelines - Canada.ca
[6] Departmental Results Report