BIOTECanada

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Dr. Mitchell Levine, Chairperson
Patented Medicine Prices Review Board
Box L40
Standard Life Centre
333 Laurier Avenue West, Suite 1400
Ottawa, Ontario, K1P 1C1

Submitted electronically: *PMPRB.Consultations.CEPMB@pmprb-cepmb.gc.ca*

Dear Dr. Levine:

On behalf of the members of BIOTECanada, I am submitting this response to the request for written comments on the draft Patented Medicine Prices Review Board (PMPRB) Guidelines issued on November 21, 2019. Our members are investing significant time and effort in assessing the impacts of the draft Guidelines on the prices of new and existing medicines. Based on this analysis we have significant concerns about the draft Guidelines as written.

BIOTECanada is the national trade association representing Canada's biotechnology industry. The 230 member companies of BIOTECanada are reflective of the broad and diverse Canadian biotechnology ecosystem which stretches across the country and includes: world-class universities and research institutes, Small and Medium Sized Enterprises (SMEs), entrepreneurs and large multinational players, all of which are supported by a highly skilled and educated workforce. All told, the Canadian biotech ecosystem is an economic strength that positions Canada well to successfully compete in the emerging global bio-economy.

The past 30 years have seen many advances in biotechnology resulting in Canadians living longer, more productive and higher quality lives today. Now, stem cell, gene and cell therapies, immuno-oncology therapeutics, CRISPR editing and new vaccines hold the promise of cures for many more diseases, including rare diseases. Canadian regulatory policies must enable and support Canadian patients' timely access to these state-of-the-art treatments.

BIOTECanada is very concerned that regulatory amendments and implementation of the draft Guidelines in their current form will have far-reaching negative real-world impacts on the Canadian biotechnology industry, research and investment in the Canadian economy, and industry funding of important services such as patient support programs, and clinical trials. Regulatory and policy changes of this magnitude must be carried out in accordance with the PMPRB's own mandate and Consultation Policy[1], which is based on the principles of fairness, transparency, openness, and predictability.

[1] PMPRB Consultation Policy http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1028&lang=en

The Industry's principal areas of concern are:

- **Lack of meaningful consultation**, disregard for industry input offered to date, and the need for significant, meaningful parallel technical consultation between the PMPRB and patentees prior to the implementation of the new Guidelines to ensure they are workable and grounded in commercial reality.
- **Confidentiality and globally non-competitive price uncertainty concerns** jeopardizing patient access to the next generation of breakthrough treatments in Canada, including life-saving oncology therapies, vaccines and drugs for rare diseases.
- **Multiple technical issues** related to the real-world application of the draft Guidelines. These concerns are outlined in the attached Appendix – Detailed Technical Feedback.

Thorough and Meaningful Consultation

The PMPRB has failed to provide clarity on several questions raised by the industry and other stakeholders. Correspondingly, there remain numerous uncertainties with respect to the Guidelines, as evidenced in the attached Detailed Technical Feedback. BIOTECanada members have been actively engaged throughout the PMPRB Reform process to date, notwithstanding PMPRB Staff's stated perception that our engagement has not always been meaningful. BIOTECanada has made three written consultation submissions[2] on the proposed reform since 2016, and BIOTECanada member representatives sat on the Steering Committee from 2018 through mid-2019. Important points have been raised by industry members both in-person and in writing on the expected impact of the changes and the very serious implementation issues and oversights. So far, PMPRB has ignored these concerns and largely avoided substantive discussions. The draft Guidelines have also disregarded much of the feedback and recommendations contributed by the Steering Committee. BIOTECanada member companies view these Guidelines consultations as vital to improving the draft Guidelines proposal and providing manufacturers and other stakeholders with increased certainty regarding their implementation and enforcement.

The intended timeline for consultation on these draft Guidelines is insufficient, and implementation of the Guidelines should be delayed to allow for a thorough and meaningful examination of alternatives. There is no need to rush implementation of new Guidelines by July 1, 2020, as compliance with the new Patented Medicines Regulations can be accomplished in their absence. Substantial unresolved questions and inconsistencies remain and will undermine the implementation of the framework and ultimately negatively impact healthcare options for Canadians. Effective, committed and detailed biopharmaceutical industry input is vital to this Guidelines development process. The industry has offered significant effort to constructively contribute to the consultations. The dismissal of this input raises serious concerns that the PMPRB is actively choosing to ignore stakeholder views. Given the importance of ensuring access to medicines for Canadian patients, the façade of a consultation is no substitute for an actual meaningful engagement. To this extent, we strongly urge the PMPRB to review its approach and undertake a meaningful consultation process, including the immediate establishment of Technical Working Groups to reshape and refine the proposed draft Guidelines.

[2] BIOTECanada Submissions to PMPRB http://www.biotech.ca/policy-matters/health/

Confidentiality Concerns

Some aspects of the proposed draft Guidelines erode the confidentiality of sensitive commercial information. In particular, CADTH and INESSS are moving to report the results of economic analyses in such a way that anyone will be able to calculate the Pharmacoeconomic Price (PEP), rendering the Maximum Rebated Price (MRP) essentially transparent. This is completely inconsistent from the procedures seen in other international jurisdictions. While it is true other jurisdictions may use general thresholds that are widely known (cost-effectiveness, budget impact, etc.), these thresholds are a starting point for payer-manufacturer negotiations as opposed to a mandated price ceiling. These thresholds are also variable based on the specific attributes of a given product and the clinical context of the underlying disease or condition it treats. No other international jurisdictions' system publishes data that would enable the manufacturers' competition to accurately calculate the prevailing confidential rebated prices. These confidentiality disclosure concerns may lead manufacturers to prioritize other international launches ahead of Canada, thus jeopardizing timely access to medicines for Canadians.

Globally non-Competitive Pricing Uncertainty and Impact

The introduction of the PEP and ongoing price reassessment, as conceived in the draft Guidelines, causes unacceptable price uncertainty for the industry, and will mean Canada's ability to compete in the global biotechnology and pharmaceutical landscape for timely access to breakthrough treatments will be diminished.

Pharmacoeconomic models are inherently uncertain, as they are built on many assumptions of key variables. The CADTH base case incremental cost-utility ratio (ICER) usually varies significantly from the manufacturer-submitted base case ICER, and CADTH economic reviewers manipulate the model assumptions with the express goal of reducing potential payer risk. Oftentimes these assumptions are so skewed towards payer risk-aversion they are unrealistic. Manufacturer comments on the reanalyzed ICER values are limited and not always shared with the expert reviewer committees to inform their deliberations. The modified analyses are not shared with manufacturers, so it is usually not possible for patentees to faithfully replicate CADTH's changes and therefore adequately understand or refute the reanalysis. It is also noteworthy that CADTH and INESSS often report very different ICERs for the same product, beyond what can be explained by the differences in economic model perspectives between the two agencies. Furthermore, reliance on CADTH or INESSS models to regulate prices essentially extends the PMPRB's quasi-judicial process (including any future PMPRB hearings) to encompass CADTH and INESSS staff and economic reviewers. Two Quebec Ministers have provided written feedback that they believe PMPRB's use of economic models in this way is inappropriate.

Pharmacoeconomic models are particularly limited in their ability to inform HTA decision making for drugs that treat rare disorders. The draft Guidelines propose a pharmacoeconomic price multiplier for rare diseases, but the value of this apparent concession is diminished by the application of a lower threshold for market size rebates for this category of drugs.

The proposed Guidelines introduces several reassessment measures and a complex process for re-categorization of products following initial launch, which limits the predictability of list and rebated prices over time. This uncertainty will influence manufacturers' decisions to invest in clinical or patient support programs or endorse long-term research initiatives in Canada.

These issues, along with those highlighted in the attached *Appendix – Detailed Technical Feedback*, lead to extreme price uncertainty and real concern the proposed Guidelines are intended to force Canadian prices to a level significantly below international jurisdictions with comparable health systems. In this environment, global and local companies will have no choice but to alter their marketplace strategies. We are aware of new breakthrough biotechnology treatments whose Canadian filings are already being delayed because of the price uncertainty created by the proposed changes. We also know of other scenarios where biopharmaceutical companies are questioning the viability of future Canadian product launches.

The impact of this unpredictability and concern about mandated ceilings on rebated prices is greatest for the most innovative breakthrough therapies including medicines such as first in class drugs and drugs for rare diseases, as a high proportion of these drugs are likely to be designated as Category I, high priority medicines. Taken together, all of these issues and uncertainties will reduce timely access to the best medicines for patients, including access to leading edge clinical trials. This runs counter to Health Canada's stated goal of improving access to drugs, alongside improved affordability.

BIOTECanada recognizes and supports Health Canada's goals of accessibility, affordability and appropriateness in the provision of medicines to Canadians. We would like to re-iterate that the proposed regulatory and policy changes proposed by the PMPRB must be carried out based on the principles of fairness, transparency, openness, and predictability; the industry is concerned these important principles were not followed during this process. We are prepared to work collaboratively with the PMPRB to achieve reform that will ensure affordability without the level of uncertainty and risk in the current proposed approach.

Sincerely,

Andrew Casey
President & CEO

Enclosures

BIOTECanada

Appendix – Detailed Technical Feedback

Section 1: General Comments

To date, consultation on the draft PMPRB Guidelines has been insufficient, and there are many significant practical implementation issues with the draft as presented, some of which are insurmountable. It is important to ensure the appropriate amount of time is set aside to address the complex issues raised by the proposed Guidelines. By ensuring the Guidelines are implemented appropriately, less regulatory burden will be realized by the PMPRB, patentees, and other impacted parties. In order to resolve these issues and refine the draft Guidelines, several Industry/PMPRB Staff technical working groups should be formed and deliberate on the changes prior to Guideline finalization.

In years past, the PMPRB worked to uphold the principles of fairness, transparency, openness, and predictability. The proposed reforms appear to move the PMPRB away from this principled approach; we respectfully ask that the PMPRB re-examine its approach to realign itself with its historical direction. Six general areas of concern for BIOTECanada members that demonstrate the PMPRB's potential departure from its core principles are the following:

- Uncertainty
- Confidentiality
- Pharmacoeconomic Value
- Market Size Adjustment
- Role of HDAP/Consideration of Level of Innovation in determining MLP
- Cases requiring special consideration

Additionally, the proposed approach deviates from the proper mandate and role of PMPRB, ensuring prices of patented medicines are "non-excessive" and instead moves toward regulation of both list and net prices to the lowest level, internationally, and inappropriately intrudes into the role and mandate of third-party payers, including the provinces and territories.

Uncertainty

At their core, the proposed Guidelines reduce the certainty patentees now have regarding how to operate a business in a compliant manner throughout the lifecycle of a patented medicine. This is best demonstrated by the following statement found in Section II(5) of the Guidelines:

> *In accordance with subsection 96(4) of the Act,* ***these Guidelines are not binding on Staff,*** *the Chairperson, Hearing Panels or patentees, and are not intended to create any legal rights or presumptions, to restate the law or to constitute a definitive statement on the interpretation of the legislation related to the PMPRB. The enforcement decisions of Staff and the ultimate resolution of issues will depend on the particular circumstances of the matter in question. Final interpretation of the law is the responsibility of the Board (sitting as a Hearing Panel) and the courts. [Emphasis added]*

In addition to the ambiguity created by this change to how Board Staff is to use the Guidelines, the new Guidelines now integrate modeled data that is entirely dependent on assumptions to define net price ceilings in Canada. Specifically, market size estimates generated by patentees will be used to categorize drugs while pharmacoeconomic evaluations generated by Canadian Health Technology Assessment (HTA) agencies will be used to establish net price ceilings. These will be explored further later in this text.

The proposed Guidelines introduce several reassessment measures and a complex process for re-categorization of products, meaning prices will be subject to serial downward reassessments of unknown magnitude while the medicine is patented. This price and revenue uncertainty will likely impact patentees' ability and interest to invest in programs or support long-term initiatives. This price/investment trade-off is most clear with generic vs. patented medicines but can also be seen in lower levels of investment in patient services by biosimilar manufacturers, as compared to brand originators. PMPRB must reconsider the value of ongoing unpredictable price reassessment of medicines, and the high likelihood that the Canadian pricing environment will be viewed as the most complex jurisdiction in any developed pharmaceutical market.

Confidentiality

The confidentiality of Canadian net prices must not be compromised, or multi-national companies will de-prioritize Canadian launches and investment, and smaller companies that would otherwise launch in Canada will choose not to, to protect the value of the US market. The current PMPRB proposal will allow domestic and foreign competitors to calculate the ceiling net price of new product and/or indication launches in Canada. While some level of net price transparency may exist in other international markets, the reduction in price is negotiated in the context of National public reimbursement, and negotiations often bring in other factors that make it difficult to calculate confidential rebates. Furthermore, unlike markets in other parts of the world, Canada shares a border with the world's largest pharmaceutical market (i.e., United States). With the threat of US importation of Canadian pharmaceuticals constantly increasingly, global organizations may choose to optimize their business strategies in a manner that works against Canadian access to and supply of medicines.

Pharmacoeconomic Value

BIOTECanada members strongly oppose the application of pharmacoeconomic value assessment to set prices. If pharmacoeconomic models are to play a future role in pricing, patentees must have the opportunity to present evidence to refute the application of inappropriate methods and/or assumptions in any CUA prepared by a Canadian HTA agency that would be used to establish the PEP/MRP. As it stands, there is no independent expert arbitrator that can be consulted when industry and CADTH/INESSS disagree regarding the clinical applicability of specific modeling assumptions, despite the fact that assessments conducted by these agencies now carry legal weight.

Market Size Adjustment

Price adjustments based on market size are a form of revenue control, not price regulation, and therefore are beyond the PMPRB's jurisdiction. Further, the proposal to reduce the net price ceiling of products based on increased market size while not allowing for the option to raise the net price ceiling of products should their market size decrease is not aligned with the PMPRB's basic principle of fairness. By not allowing for the net price ceiling to fluctuate, the PMPRB is creating a system that will result in market distortions that will rapidly deteriorate the value of transformative medicines such as high-impact single and short-term therapies (e.g., cell therapies, gene therapies).

Role of HDAP/Consideration of Level of Innovation in determining MLP

The role of HDAP is not defined in these draft Guidelines, and is referred to only in Section XIII(A) in the context of Staff seeking "...non-binding advice" from HDAP "...in some cases" regarding the selection of comparators for domestic and/or international Therapeutic Class Comparison (TCC) tests. BIOTECanada recommends HDAP play a similar role as, under the new Guidelines, as they do currently. This would include establishment of a primary indication (where applicable), identification of relevant comparators and comparable dosing regimens, and level of therapeutic improvement.

Although the level of therapeutic improvement has been removed from the tools to be used to establish the price of medicines, BIOTECanada recommends that it be reintroduced. Without such a revision, the proposed Guidelines will create market distortions that allow for a new medicine that is a substantial improvement to all other comparable medicines to be priced below the price of some of its inferior counterparts.

Transformative Therapies

The proposed Guidelines appear to have been developed based on historical trends and experience rather than forward looking toward the future. The market dynamics of newer treatments, including cures, will not necessarily follow these traditional trends. The guidelines, in their current form, will disadvantage the Canadian market versus other international markets as new transformative medicines are launched around the world. To avoid this scenario, it is important for the PMPRB to establish working groups to identify appropriate methods for addressing these emerging technologies.

The proposed guidelines will undermine the entry of single or short-term transformative therapies (SSTs) into the Canadian market. These treatments include one-time treatments such as cell therapy and gene therapy, as well as potential cures like those offered to HCV-infected patients. The Institute for Clinical and Economic Review (ICER) group, with support from CADTH and NICE, has recognized the unique challenges associated with these types of treatments and has taken steps to find a solution that is appropriate for the American healthcare system.[1,2] BIOTECanada believes similar work is required here in Canada to create a solution that works for Canadian patients and payers.

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[1] https://icer-review.org/methodology/icers-methods/icer-value-assessment-framework-2/
[2] https://icer-review.org/topic/valuing-a-cure/

In the coming age of SSTs, society will benefit from curative therapies that will require an initial payment to treat the prevalent population followed by a rapid decline in healthcare spending as more patients are cured. SSTs require short-term spending; however, the benefits are expected to last for a lifetime. We understand the need for a sustainable healthcare system in Canada, but sustainability will not be achieved by relying on simple price reductions.

It is now more important than ever that Canadian health policy evolve to support the launch and reimbursement of highly innovative products. As proposed, the draft PMPRB Guidelines will run counter to the objective of making Canada a preferred country to launch new therapies. As has been noted in the literature, the challenges posed by the initial price of SSTs can be overcome in a number of creative ways that consider long-term affordability beyond price. This includes the amortization of costs over a longer timeframe or the implementation of outcomes-based agreements.

It is increasingly likely that new innovative therapies will be used in combination, and the proposed PMPRB Guidelines do not account for this. When a treatment regimen comprised of multiple treatments is submitted to CADTH/INESSS, the resulting ICER will be for the treatment combination. It is unclear how the proposed Guidelines will ascribe value to multiple drugs in a combination drug treatment regimen.

Reanalysis of many publicly available economic reviews published by CADTH, based on the draft Guidelines, would result in very low or even negative PEPs. Such results are nonsensical and indicate that the PEP methodology does not appropriately account for the fact that all medicines approved by Health Canada have a positive risk-benefit profile, and therefore, some economic value, or the fact that pharmaceutical manufacturers are commercial enterprises that must recoup investments and manufacturing costs through their price strategies.

Section 2: List of Detailed Comments and Recommendations:

BIOTECanada membership is strongly opposed to the use of pharmacoeconomic value and market size as pricing tools, and to the PMPRB having a role in setting net price ceilings. The comments and recommendations below should not be construed as agreement with the regulatory framework.

Comment No.	Line No.	Section	Text from Draft Guideline	Key issues/ Question for clarification	Proposed Revised Text (in **bold**) and Recommended Next Steps
1.	1 - 3	I	Entire Preface	The guidelines are ambiguous and do not allow patentees to reliably predict the allowable ceiling (MLP or MRP) at launch or throughout the product lifecycle. Major sources of uncertainty include: • use of median dTCC (selection of comparators by the PMPRB, timing of new entrants on the market, including generics, lack of clarity with respect to how the comparators and their prices will be defined); • use of economic factors (no predictability on the CADTH re-calculated ICER or whether their CUA is "useable"); • broad criteria for reassessment (including factors beyond patentees' control); and • changes to market size and Pharmacoeconomic thresholds	Establish bilateral PMPRB/Industry working groups, with Industry representatives chosen by IMC and BIOTECanada to refine the draft Guidelines to reduce uncertainty in Canadian pharmaceutical prices and ensure the Guidelines can be practically implemented.
2.	2, 3, 6, 21, 25, 88, 90	I, III, IV, X	The reference to "any market in Canada" in several sections of the Guidelines, including the Preface, Legal Framework, Filing Requirements Pertaining to Price Reviews, and Excess Price Hearing Process and Remedies	In the absence of an updated Patentees' Guide to Reporting, and any reference within the Guidelines to how sales data will be filed, the definition of "any market in Canada" is unclear. It is essential that the Patentees' Guide to Reporting, or some similar documentation be updated in parallel with Guideline finalization	Establish a working group to determine the definition of "any market in Canada" and reflect this consensus definition in the final Guidelines and/or a document similar to the current Patentees' Guide to Reporting. This guidance document must be provided to patentees well in advance of implementation of any new Guidelines to give patentees time to change their

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				to ensure that all implementation issues are resolved prior to implementation of the new Guidelines. This information should be available at least 6 months prior to application of any new Guidelines.	reporting and administrative systems to accommodate the new requirements.
3.	5, 8	II	"[...]these Guidelines are not binding on Staff" "[...] In no case will Staff or Board members be bound or limited by these Guidelines."	Permitting the Staff and Board to apply tests and methods not contemplated elsewhere poses unacceptable level of uncertainty and unpredictability to patentees. Certainty and predictability are essential to business decision making. Given the degree of uncertainty inherent in the current draft of the Guidelines, companies are, and will make decisions to delay or cancel regulatory filings in Canada. The level of uncertainty and unpredictability in these draft Guidelines would not be considered acceptable for any industry operating in Canada. Implicit in the existing Guidelines language, and explicit in their application is the principle that Board Staff are bound by the Guidelines, while the Board and patentees are not. Existing Guidelines Preamble: "One of the primary objectives of the Compendium of Policies, Guidelines and Procedures (Compendium) is to ensure that patentees are aware of the policies, guidelines and procedures under which Board Staff reviews the prices of patented drug products sold in Canada, and the procedures normally undertaken in the scientific and	"[...] In no case will ~~Staff or~~ Board members or patentees be bound or limited by these Guidelines."

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				price review processes and when a price appears to be excessive." A.3.5: "Board Staff carries out the day-to-day work of the PMPRB including the administration of the Patented Medicines Regulations (the Regulations) to ensure compliance with the prescribed filing requirements. The review of prices of patented medicines is carried out in accordance with the Guidelines, which are approved by the Board." A.5.3: "The Board, following considerable deliberation and consultation with all stakeholders, pursuant to subsection 96(5) of the Act, published the PMPRB's Guidelines pursuant to subsection 96(4) of the Act. Although the Guidelines are not binding on the Board or the patentee, they establish an approach and methodology in applying the factors set out in subsection 85(1) of the Act."	
4.	13	III	The PMPRB maintains an arm's length relationship from the Minister of Health (who is responsible for the sections of the Act pertaining to the PMPRB), the Minister of Innovation, Science and Economic Development (who is responsible for the Act as a whole) and its various stakeholders.	The Minister of Innovation, Science and Industry is the new title for the Minister responsible for the Patent Act.	The PMPRB maintains an arm's length relationship from the Minister of Health (who is responsible for the sections of the Act pertaining to the PMPRB), **the Minister of Innovation, Science and Industry** (who is responsible for the Act as a whole) and its various stakeholders.

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6	17	III	An invention pertains to a medicine if the invention is intended or capable of being used for medicine or for the preparation or production of medicine. The phrase "pertain to a medicine" has a broad meaning. The Federal Court of Appeal has determined that the nature of that connection may be "tenuous". It is satisfied, for example, where there may "only be a slender thread of a connection between a patented invention and the medicine sold in Canada"	To the contrary, the Federal Court of Appeal (7/2019 Attorney General) v. Galderma Canada Inc. 2019) concluded that PMPRB incorrectly applied the patent-pertaining analysis in the case concerning Differin (Galderma). The Court's decision challenged the prior practice of the Board to take jurisdiction over patents based on 'any mere' reference to the medicinal ingredient, including only a reference in the disclosure. The PMPRB has pulled this statement out of context of the full Ruling on the issue. See below: *"The expression "merest slender thread" is a metaphor designed to express the idea that the connection may be tenuous. While it is true that the expressions "pertaining to" and "pertains to" express a looser association than might be conveyed by other more restrictive expressions (such as an invention "comprising" a medicine), those expressions must be understood in context."* *It goes without saying that the metaphor which describes the relationship expressed by "pertains to" cannot supplant the statutory definition of that expression. This is not to say that the metaphor is not a useful way of expressing the possibility that the relationship between the invention and a medicine may*	An invention pertains to a medicine if the invention is intended or capable of being used for medicine or for the preparation or production of medicine. ~~The phrase "pertain to a medicine" has a broad meaning. The Federal Court of Appeal has determined that the nature of that connection may be "tenuous". It is satisfied, for example, where there may "only be a slender thread of a connection between a patented invention and the medicine sold in Canada"~~

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				be tenuous but, at the end of the day, the question is whether the invention is intended or capable of being used for medicine, and not whether there is the merest slender thread of a connection."	
8.	25	IV	"Information that patentees or former patentees may be required to file under the Regulations includes, but is not limited to: [...]	There are few details given regarding information filing, specifically timelines for CUA submission and details of how to define "maximum use" of the medicine. In addition, there is reference to "a given time period" for the maximum use of the medicine and this is not defined. While the list of requirements is not intended to be fully inclusive, it does not explicitly outline reporting of prices and revenues net of rebates. BIOTECanada members assume this reporting requirement will exist, but it is not reflected in the Patented Regulations or these draft Guidelines. Clarification of this reporting required is required. It is our understanding that estimated maximum market size will be based on forecast units multiplied by list price for the first 3 years of sales. List prices should not be used if the forecasted volumes could include free goods and/or discounted sales.	A working group should be formed to develop consensus on the details of reporting requirements and to support the development of and/or a document similar to the current Patentees' Guide to Reporting.
9.	29	IV	The Act provides for the confidentiality of information	The derivation and application of an MRP using either PEP methodology (with publicly	BIOTECanada members strongly object to the use of pharmacoeconomic value to

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			supplied to the PMPRB in certain circumstances. Specifically, information or documents provided to the PMPRB in accordance with the provisions dealing with pricing information in sections 80, 81 and 82 of the Act, or in any proceeding relating to excessive prices under section 83, is privileged and cannot be disclosed to the public without authorization of the disclosing party, unless such information has been disclosed at a public hearing under section 83 of the Act or is subject to the exceptions outlined in section 87(2) of the Act	available inputs) or dTCC contravenes confidentiality; this will either create public awareness of net price levels in a class or competitive manufacturer awareness. Use of pharmacoeconomic value based on an ICER threshold to set a price ceiling will have significant unintended negative consequences for the Canadian pharmaceutical industry and Canadian patients.	establish MRP. It is recommended that a working group be formed to discuss alternatives to use of CUA to set price ceilings.
10.	25	IV	Information that patentees or former patentees may be required to file under the Regulations includes, but is not limited to: ... Prescribed information relating to cost-utility analyses prepared by publicly funded Canadian health technology assessment (HTA) agencies, for which the outcomes are expressed as the cost per quality-adjusted life year (ICER) for each indication that is the subject of the analysis; and [...]	Per Regulations, this is only a reporting requirement if treatment cost (per CUA, "the analysis") greater than or equal to 50% of GDP per capita BIOTECanada's understanding is that Category I medicines product with a low annual cost (<50% of GDP/capita), and thus no submitted ICER, will not have a PEP and market size rebates will be calculated based on the MLP.	As per the Patent Act and the Amendments to the Patented Medicines Regulations, information that patentees or former patentees may be required to file under the Regulations includes, but is not limited to: ... Prescribed information relating to cost-utility analyses prepared by publicly funded Canadian health technology assessment (HTA) agencies, for which the outcomes are expressed as the cost per quality-adjusted life year (ICER) for each

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					indication that is the subject of the analysis; and [...]
11.	38	V(A)1	The iMLP will be recalculated annually and will apply until the earlier of: (i) three (3) years from the date of the introduction of the patented medicine in Canada; or (ii) the date when the patentee has filed international price information for at least five (5) of the PMPRB11 countries. At the end of the interim period, the MLP will be set (see Step 2) and the iMLP will cease to apply.	Changing list prices is not a simple process and has implications for the entire pharmaceutical supply chain. It is impractical to change list prices multiple times over a 3-year period. As a benchmark, the iMLP should increase or decrease during the interim period, contrary to the strict application of the language of the draft Guidelines. Further clarity is required around how changes to the iMLP will be implemented, and when. As written, the draft Guidelines imply at least annual, or perhaps even more frequent list price changes. This is unworkable for patentees, payers and the entire pharmaceutical supply chain.	Clarification that the iMLP needn't be changed until the end of the interim period, and/or that it can track upwards or downwards over time.
12.	39	V(A)2	[...] but is subject to a price floor set by the lowest international price ("LIP") for the PMPRB11 countries for which the patentee has provided information at the end of the interim period	If the MLP is set at the LIP, and the LIP rises over time, patentees should be re-set to the new LIP.	Add new section – line 43, as follows: "43: If the MLP was set by the LIP and, in subsequent periods, the prevailing LIP exceeds the MLP, the MLP may be adjusted to the new value of the LIP."

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13.	39	V(A)2 MLP new products	Subject to the procedure described above, the iMLP will be replaced by a **Maximum List Price** (**"MLP"**). The MLP will be set by the lower of the MIP or the median domestic Therapeutic Class Comparison (**"dTCC"**) but is subject to a price floor set by the lowest international price (**"LIP"**) for the PMPRB11 countries for which the patentee has provided information at the end of the interim period.	Setting MLP at the lower of the dTCC or MIP does not recognize nor reward innovation, particularly since the dTCC is defined by the median (not highest) of the comparator basket. A product with superior efficacy/safety vs. its comparators would be assigned a lower price (median of the dTCC) than those inferior comparators.	Replace all references to median dTCC in the Guidelines with highest non-excessive dTCC.
14.	42,59	V(A)2, V(B)	If the MLP is set by the MIP and, in subsequent periods, the prevailing MIP exceeds the MLP by more than 10%, the MLP may be adjusted based on actual lagged CPI, as long as the MLP does not exceed the MIP. The MLP may also be subject to reassessment if it is set by the MIP and, in subsequent periods, the prevailing MIP is lower than the MLP by more than 10% (see section VI).	This section does not clarify the impact of changes in the MLP if it is set by the NEAP/MAPP, or the dTCC. There is also no rationale given for the +/-10% threshold. What is the rationale for selecting 10% as the value for an upward or downward MIP to MLP adjustment? What if the MIP=LIP? Would the floor require the price to increase at a rate above that of CPI?	A working group should be formed to develop consensus on the details of all aspects of implementation of the MLP and to support the development of and/or a document similar to the current Patentees' Guide to Reporting

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15.	49	V(A)	A patented medicine will be classified as Category I if it meets either of the following criteria: 12-month treatment cost greater than 50% of GDP per capita: following the filing of introductory period pricing information, the medicine's 12-month treatment cost will be calculated by Staff based on the maximum dosage per course of treatment listed in the product monograph; the maximum number of courses of treatment per 12 months, based on the nature of the condition, clinical practices, and other relevant criteria; and the highest Canadian List Price. If a List Price is not available, the national Net Price will be used. Estimated or actual market size (revenue) exceeds annual Market Size Threshold: the annual Market Size Threshold will initially be set at $25 million.	Category I should only be set based on the cost being greater than 50% of GDP per capita at launch. Market size should only trigger movement from Category II to Category I if the actual sales in reporting year exceed the threshold for that year. Evaluation should only occur for the first three years after launch. It should be possible for Category I medicines to be reclassified as Category II based on actual data. Market size adjustments should not penalize patentees due to transient, unforeseen market events (e.g., drug shortages). Estimated market share should be used to put a drug on a watch list. If a patentee's CUA can't be used for price setting, its forecast should not be used.	A patented medicine will be classified as Category I if it meets either of the following criteria: 12-month treatment cost greater than 50% of GDP per capita: following the filing of introductory period pricing information, the medicine's 12-month treatment cost will be calculated by Staff based on the maximum dosage per course of treatment listed in the product monograph; the maximum number of courses of treatment per 12 months, based on the nature of the condition, clinical practices, and other relevant criteria; and the highest Canadian List Price. If a List Price is not available, the national Net Price will be used. ~~Estimated or a~~ Actual market size (revenue) exceeds annual Market Size Threshold **in any of the 3 years following the launch of the medicine**: the annual Market Size Threshold will initially be set at $25 million.

Comment No.	Line No.	Section	Text from Draft Guideline	Key issues/ Question for clarification	Proposed Revised Text (**in bold**) and Recommended Next Steps
16.	49	V(A)	[...] the medicine's 12-month treatment cost will be calculated by Staff based on the maximum dosage per course of treatment listed in the product monograph; the maximum number of courses of treatment per 12 months, based on the nature of the condition, clinical practices, and other relevant criteria; and the highest Canadian List Price."	The initial Canadian list price may be the iMLP, which could be higher than the MLP. As such, if the treatment cost exceeding 50% GDP per capita was the determining factor in classification to Category 1, a drug could have been classified as such prematurely. More details are required to guide this assessment for drugs that may have variable treatment durations, for example, oncology drugs that are used continuously or episodically until disease progression. The regulations state that (4.1(5)): "An analysis [CUA] shall be provided to the Board only if any cost for the medicine as identified in the analysis is or would be, when that cost is pro-rated to account for that medicine's use over a 12-month period, greater than or equal to 50% GDP per capita at time of publication of analysis" There is a discrepancy between this section of draft Guidelines and the Regulations, as the Guidelines state that that the product monograph will be used to calculate the 12-month treatment cost. Please confirm that the MRP for a Category I medicine with annual cost less than GDP/capita, will not have a PEP, and will only be subject to an MRP if and when annual revenues exceed $25 million per year.	[...] the medicine's 12-month treatment cost will be calculated by Staff based on the maximum dosage per course of treatment listed in the product monograph; the maximum number of courses of treatment per 12 months, based on the nature of the condition, clinical practices, and other relevant criteria; and **the lower of the MLP and the highest compliant** Canadian List Price." 12-month treatment cost greater than 50% of GDP per capita: following the filing of introductory period pricing information, the medicine's 12-month treatment cost will be **obtained from the submitted CUA. If the CUA is not available, the cost will be** calculated by Staff based on the maximum dosage per course of treatment listed in the **'Dosage and Administration' section of the** product monograph; the maximum number of courses of treatment per 12 months, based on the nature of the condition, clinical practices, and other relevant criteria; and **the lower of the MLP and** the highest Canadian List Price. If a List Price is not available, the national Net Price will be used. Estimated or actual market size (revenue) exceeds annual Market Size Threshold: the annual Market Size Threshold will initially be set at $25 million

Comment No.	Line No.	Section	Text from Draft Guideline	Key issues/ Question for clarification	Proposed Revised Text (**in bold**) and Recommended Next Steps
17.	32 &50	V(A) Backgro under	Guidelines: "As an initial review step, patented medicines are divided into: (i) the dosage strengths and forms for patented medicines which received a Drug Information Number (DIN) prior to August 21, 2019 ("grandfathered" products); and (ii) all other dosage strengths and forms of patented medicines which had not received a DIN as of August 21, 2019." Guidelines: "All other patented medicines will be classified as Category II. This includes line extensions of grandfathered patented medicines to which a DIN was assigned on or after August 21, 2019, where the DIN does not relate to a new indication" Backgrounder: "line extensions of existing products that are assigned a DIN after August 21, 2019 are not grandfathered even though the original related products existing prior to August 21, 2019 are"	This means that new DINs of grandfathered medicines, approved for the same indication will be limited to an MLP that is the lower of MIP11, dTCC, or LIP. Because the grandfathered medicine is limited to an MLP the lowest of MIP11 or NEAP/MAPP, this will result in DINs of the same molecule and same indication with different price structures. This is extremely difficult and, in some cases, impossible for patentees and/or payers to operationalize. Also, it is unclear from the draft Guidelines whether a new DIN of a grandfathered medicine can ever trigger a reassessment of the grandfathered DINs.	"All other patented medicines will be classified as Category II **and be treated the same as the grandfathered product.** This includes line extensions of grandfathered patented medicines to which a DIN was assigned on or after August 21, 2019, where the DIN does not relate to a new indication." **New DINs of existing grandfathered medicines have an MLP set by the RRT.** **Use the language from the existing PMPRB Guidelines to define the options for the RR test.**

Comment No.	Line No.	Section	Text from Draft Guideline	Key issues/ Question for clarification	Proposed Revised Text (**in bold**) and Recommended Next Steps
18.	50	V(A)3a)	All other patented medicines will be classified as Category II. This includes line extensions of grandfathered patented medicines to which a DIN was assigned on or after August 21, 2019, where the DIN does not relate to a new indication.	The information re: line extensions needs to be clarified, particularly those that are line extensions of grandfathered products. Specifically: • New DIN(s) that exceed market size threshold or annual cost threshold (no new indication) • New DIN(s) + new indication for all DINs (either at the time of the new DIN or at a later time period) • New DIN(s) with a new indication only for the new DIN(s) • It is unclear whether <u>all</u> new DINs of grandfathered patented medicines (that do not have a new indication) are automatically classified as Category 2, regardless of annual cost or net revenue. • If a new DIN of a grandfathered product is considered a Category 2 drug, can it be reclassified as Category 1 based on market size? Is it possible to have different pricing rules for grandfathered DINs (MLP) and new DINs of grandfathered products (MLP & MRP)? • How would a pediatric formulation be treated (new strength, new pediatric indication but same use as grandfathered DINs)?	A bilateral Technical Working Group should be established to discuss the various line extension scenarios and work together to develop more robust Guideline recommendations

Comment No.	Line No.	Section	Text from Draft Guideline	Key issues/ Question for clarification	Proposed Revised Text (**in bold**) and Recommended Next Steps
19.	51	V(A)3a) *sic*	Entire Section		BIOTECanada members strongly object to the use of pharmacoeconomic value to establish MRP. We recommend a working group be formed to discuss alternatives to use of CUA to set price ceilings.
20.	51	V(A)3 a) sic	For patented medicines with an estimated total prevalence no greater than 1 in 2,000 across all approved indications, the MRP will be set at 50% above the PEP, but will be further adjusted for market size if the patented medicine realizes annual revenues in excess of $12.5 million (see Appendix D, "Market Size Adjustment Methodology").	Presumably, including a higher PEP is intended as a price concession for rare disease medicines. However, it is unclear whether the price concession will be applied to rare disease medicines with expected net revenues >$25M. Also, the application of a lower market size threshold for rare disease medicines ($ 12.5K) will mean that PEP concession offers very little value to patentees in practice.	A working group should be formed to develop consensus on assessing drugs for rare diseases.
21.	52	V(A)3a)	If the procedure above results in an MRP that exceeds the MLP, the MRP will be set at the same level as the MLP	If the MRP has a ceiling, it should also have a floor	If the procedure above results in an MRP that exceeds the MLP, the MRP will be set at the same level as the MLP. **If the procedure above results in an MRP that is below the LIP, the MRP will be set at the same level as the LIP**

Comment No.	Line No.	Section	Text from Draft Guideline	Key issues/ Question for clarification	Proposed Revised Text (**in bold**) and Recommended Next Steps
22.	53	V(A)3b)	If a patentee does not file a cost-utility analysis prepared by a publicly funded Canadian organization for a Category I patented medicine, or if the analysis submitted does not allow for the determination of the MRP as described above, the MRP may be set by using alternative methods. Such methods may include, but are not limited to: The MRP being set by the lower of the LIP, the dTCC or the international Therapeutic Class Comparison ("iTCC"), with further adjustments based on the Market Size Adjustment Methodology.	The PMPRB should be limited to relying on CUAs submitted by patentee, not by a third party. If the alternative MRP method is acceptable, why not use it instead of CUA? This language should align with the Regulations	If a patentee does not file a cost-utility analysis prepared by a publicly funded Canadian organization for a Category I patented medicine, based pm 12-month treatment cost greater than 50% of GDP per capita or if the analysis submitted does not allow for the determination of the MRP as described above, the MRP may be set by using alternative methods. Such methods may include, but are not limited to: The MRP being set by the lower of the LIP, or the dTCC ~~or the international Therapeutic Class Comparison ("iTCC"),~~ with further adjustments based on the Market Size Adjustment Methodology. Cost-utility analyses that have not been submitted to the PMPRB by the patentee will not be considered when determining the MRP. Use of the iTCC should be limited to investigations and hearings, similar to the current Guidelines.
23.	55	V(A)3 b) *sic*	Once set, the MRP will be only reassessed at a later point in time if it meets the criteria set out in section VI.		A working group should be formed to develop consensus on the details of all aspects of the proposed MRP.
24.	59	V(B)	The MLP for all grandfathered patented medicines will be set at the lower of (i) the MIP for the	For grandfathered drugs, Guidelines propose setting the MLP as the lower of the MIP or NEAP/MAPP. However, the NEAP is a net	The MLP for all grandfathered patented medicines will be set ~~at the lower of (i)~~ the MIP for the PMPRB11 countries for which

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			PMPRB11 countries for which the patentee has provided information, or (ii) the patented medicine's ceiling under the Guidelines applicable prior to the issuance of these Guidelines.	price, not a list price. It is inappropriate to set a list price ceiling based on a price net of benefits.	the patentee has provided information, ~~or (ii) the patented medicine's ceiling price under the Guidelines applicable prior to the issuance of these Guidelines.~~ If the patented medicine's price under the Guidelines applicable prior to the issuance of these Guidelines was a non-compliant price, the previous Guidelines should be used to determine a compliant price prior to setting the MLP.
25.	63	VI	For non-grandfathered patented medicines, a reassessment may be conducted if any of the following situations arise: • A patented medicine (Category I or Category II) is approved for a new indication; [...]	Patentees have many questions about the application of reassessment, including, but no limited to: • Does approval of a new NOC(/c) for a new indication trigger a reassessment? • When is the MRP set for the new indication? • What happens to the old MRP before the new CADTH assessment occurs? • Is the iMLP set but the old MRP remains in effect? • What happens when a medicine is approved for a new indication in combination with a new drug (marketed by the patentee, of the existing drug, OR a different patentee OR part of joint venture? • Will a CUA for a new product, used in combination with an existing product, trigger a reassessment of the existing product?	Establish a working group to determine how reassessment will be conducted and the conditions that trigger reassessment. Comprehensive details regarding implementation of reassessment should be contained in the final Guidelines and/or a document similar to the current Patentees' Guide to Reporting..] For non-grandfathered patented medicines, a reassessment may be conducted if any of the following situations arise: A patented medicine (Category I or Category II) is approved for a new indication; A Category II patented medicine has sales exceeding the Market Size Threshold (see

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				• Are patentees required to report competitor CUAs that reference the patentees' product? It is also unclear whether Patentees' can apply for a reassessment.	Appendix D), contrary to the initial estimate filed by the patentee; or A Category I patented medicine's total prevalence across all approved indications, as estimated by Staff, increases above 1 in 2,000; or A Category I patented medicine's cost-utility analysis is updated; or **Patentees may apply for a re-benching with evidence of increased cost-effectiveness, smaller market, or a significant increase in CPI**
26.	65	VI	A Category II patented medicine receiving a new indication may be recategorized to Category I if it meets the Category I screening criteria. A patented medicine may also be recategorized from Category II to Category I if its revenues increase above the annual Market Size Threshold contrary to the initial market size estimate filed by the patentee. In either case, the category change will result in the patented medicine being given an MRP.	Please confirm that Category I medicines can be reclassified to Category II medicines if annual revenues at the MRP are < $25 million, or the total cost of the medicine at the MRP drops to <50% of GDP/capita.	Add section between lines 67 and 68, as follows: **[A Category I patented medicine may be recategorized to Category II if it no longer meets the Category I screening criteria.]**

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27.	68	VI – Timing for Compliance	Following such notice, the patentee will be granted until the next reporting period for the MLP, and until the end of the subsequent reporting period for the MRP to ensure that prices are adjusted such that the patented medicine is not priced higher than the modified price ceiling(s), failing which the price may be subject to additional review or investigation by Staff.		Following such notice, the patentee will be granted until the **end of the** next reporting period **(i.e., 6-11 months)** for the MLP, and until the end of ~~the~~**two** subsequent reporting period**s (12-17 months)** for the MRP to ensure that prices are adjusted such that the patented medicine is not priced higher than the modified price ceiling(s), failing which the price may be subject to additional review or investigation by Staff. **Extensions may be granted in exceptional circumstances (e.g., delayed or protracted pCPA negotiations, delayed invoices for rebates)**
28.	71	VII(A) Investigation criteria	the price of any dosage form or strength of a patented medicine appears to be above the corresponding applicable price ceiling by more than 5%;	BIOTECanada members believe it would be a better use of PMPRB resources to change the threshold for investigations to 10%, consistent with the threshold resetting the MLP. Also, the $ 50,000 criterion should be per DIN, not across all dosage forms and strengths.	"the price of any dosage form or strength of a patented medicine appears to be above the corresponding applicable price ceiling by more than ~~5~~**10**%;" the cumulative potential revenues earned as a result of pricing above applicable ceiling(s) ("**potential excess revenues**") appears to exceed $50,000 **for a given DIN** of the patented medicine.
29.	Appendix A	XIII(A) Page 25 dTCC	All medicines identified for comparison that have the same approved indication as the Relevant Indication of the patented medicine under review will be included in the review.	It appears the new Guidelines will limit TCC comparators to those with the same indication of a new medicine under review.	Confirm details of comparator selection criteria and process.

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30.	Appendix A	XIII(A) pg. 26 Price sources	Public sources will be used for the prices of the medicines used for comparison purposes in order to conduct a dTCC test. Provincial formularies will be the starting point in Staff's identification of public prices. The lowest public price for each of the medicines identified for comparison purposes will be used.	Relying on provincial formularies only for unit prices raises issues related to differences in how prices are reflected on some formularies, and when a product has no public reimbursement. It is unclear how generic medicines factor into the dTCC or iTCC basket. Generic manufacturers and branded manufacturers face very different cost structures and pricing restrictions. The inclusion of generic therapeutic class comparators in the dTCC or iTCC completely ignores these industry realities and will inappropriately and grossly reduce the prices of patented medicines, contrary to the Board's mandate of ensuring that the prices of patented medicines are non-excessive	~~Public sources~~ The Association Quebecoise des pharmaciens propriétaires (AQPP) price list will be used to identify ~~or the~~ prices of the medicines used for comparison purposes in order to conduct a dTCC test. ~~Provincial formularies will be the starting point in Staff's identification of public prices.~~ The lowest AQPP ~~public~~ price for each of the medicines identified for comparison purposes will be used. Generic products should be excluded from all PMPRB price tests for patented medicines.
31.	Appendix A	dTCC Price sources (pg. 26)	Public sources will be used for the prices of the medicines used for comparison purposes in order to conduct a dTCC test. Provincial formularies will be the starting point in Staff's identification of public prices. The lowest public price for each of the medicines identified for comparison purposes will be used.	There is significant lack of clarity around how generic prices and biosimilar prices will be used in calculating the median dTCC. In many mature categories with unmet clinical need, a generic or biosimilar may well set the median of the dTCC. Referencing such a price will be a strong disincentive for patentees to introduce new medicines in these types of therapeutic areas, including many serious chronic diseases in mental health, diabetes,	Replace all references to median dTCC in the Guidelines with highest non-excessive dTCC.

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				cardiovascular disease, infectious diseases, and seizure disorders.	
32.	Appendix A	*iTCC Test*, pg. 27	These costs of treatment will be ordered and the median identified for each country. In the event of an even number of comparator medicines used for comparison purposes, the median will be the simple average of the middle two costs of treatment.	There is significant lack of clarity around how generic/biosimilar prices will be used in calculating the median iTCC. In many mature categories with unmet clinical need, a generic or biosimilar may well set the median of the iTCC. Referencing a generic price will be a strong disincentive for patentees to introduce new medicines in these types of therapeutic areas, including many serious chronic diseases in mental health, diabetes, cardiovascular disease, infectious diseases, and seizure disorders	Replace all references to median dTCC in the Guidelines with highest non-excessive dTCC. Generic products should be excluded from all PMPRB price tests for patented medicines. The use of the iTCC shall be limited to providing information in the context of an investigation into apparent excessive prices.
33.	Appendix B	XIII(B) Reasonable Relationship Test	When a new strength of a medicine that is currently sold in Canada is introduced and meets the above requirements of the RR test, the MLP or MRP of the new strength will be set to be equivalent to the price per standard unit of the existing strength(s)	While it may seem complex, the RR test outlined in the current PMPRB Guidelines provides patentees with crucial pricing strategy flexibility.	Use the language from the existing PMPRB Guidelines to define the options for the RR test.
34.		XIII(C)PE Value Assessment		The PE Value Assessment is the most concerning aspect of the Guidelines for Patentees. BIOTECanada members strongly oppose the use of PE value to regulate MRP. Use of PE Value, and particularly CADTH CUAs, introduces so much price uncertainty that many BIOTECanada member companies	A working group should be formed to discuss alternatives to use of pharmacoeconomics (CUA) to set price ceilings.

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				have delayed submitting medicines for regulatory approval in Canada and are considering whether it is viable to launch new pipeline medicines in Canada. This will have serious negative consequences for Canadian patients and the Canadian healthcare system. The following is a list of questions regarding this part of the draft Guidelines • The PVT is arbitrary. Current Health Technology Assessments employ flexible thresholds based on unmet need, patient population, and other factors outside an economic analysis. • Current CADTH economic reports do not provide the information required to calculate the PEP • The most innovative, first in disease drugs will be disadvantaged by the model proposed, as best standard care (BSC) would likely be the pharmacoeconomic comparator. For most diseases without effective drug treatments BSC is usually relatively inexpensive. • The appropriate comparator for a product could change between the conduct of clinical trials and HTA. • It is unclear how PMPRB will reconcile differences between dTCC comparators and comparators used in CADTH CUAs. • CADTH reports ICER results in a probabilistic manner. It is unclear how	

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				PMPRB will derive a deterministic estimate for PEP calculations. • It is unclear which indication will be used in the PE value assessment for drugs that enter the Canadian market with multiple indications. • For CE models with multiple comparators, it is unclear which one will be used for the deterministic CUA analysis that will be used for the PEP calculation. • It is unclear how the PEP will be derived if the CADTH base case assessment is based on full indication, but reimbursement is based on much more restrictive criteria. • It is unclear how PMPRB will reassess the PEP based on new ICER, since patentees often do not submit updated CUAs to CADTH, and CADTH likely does not have the capacity to conduct those reviews. • The proposed PEP is inappropriate for medicines that are used in combination with other drugs and would likely lead to negative prices for the drug under review. • It seems possible for the PEP to be less than zero. It is unclear how PMPRB would apply such a result. • It is unclear how PMPRB would proceed with assessing a PEP for a medicine that receives a negative CADTH recommendation. • It appears patentees will not be able to challenge the way CADTH alters the base-	

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				case analysis submitted. This is unacceptable to BIOTECanada members. CADTH re-analyses of patentee-submitted CUAs are not peer-reviewed, transparent or developed to address the question of what the maximum allowable price should be.	
35.	Appendix D	XIII(D)	As described in section V of the Guidelines, a market size adjustment is applied to Category I patented medicines with quantities sold such that annual revenues would exceed $25 million across all dosage forms and strengths of the medicine (i.e., all DINs combined) when priced at the MRP(s) set by the PEP.	BIOTECanada members strongly opposed the application of market size adjustments, as they are revenue control instruments, rather than price control tools. The market size adjustment is a disincentive for manufacturers to develop new indications or launch extensions for existing medications. The selection of $ 25 million in annual sales to trigger the market size adjustment is based on "embryonic" research, based on the Backgrounder to the Guidelines, and thus seems arbitrary. It is difficult to understand why there is a need to apply further price reductions to medicines already selling at cost-effective prices. It is possible that a new medicine, selling a lower price than competitors, would be subject to market size adjustments, and this seems illogical. As presented in the draft Guidelines, the MRP only allows for reductions in price. If MRP is a	All reference to Market Size Adjustment should be removed from the Guidelines. A working group should be formed to alternatives to using market size to set price ceilings.

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				price regulation tool, it should allow for increases in price under circumstances that reducing the market size of a medicine. The market size adjustment should not be based on the PEP, as that could result in MRP adjustments that are unwarranted. For example, if a product is only distributed as free goods, PEP*Quantity sold could trigger an erroneous MRP. The market size adjustment methodology tables include every $ 25 Million increment in two ranges.	
36.	Appendix D	XIII(D) pg. 31 *Market size adjustment for Category I rare disease or disorder patented medicines*		According the draft Guidelines, a rare disease would be reclassified as "non-rare" once sales reach $25 Million, annually. Presumably, the allowance of a 50% premium over PEP is intended to incent launch of rare disease medicines in Canada, however, in reality, it is a very minor concession, and is far outweighed by the incredibly negative impact the PEP methodology will impose on rare disease medicines.	We recommend that a working group be established to resolve pricing issues pertaining to rare disease drugs and other highly innovative therapies.
37.	D		After the initial market size adjustment, a patented medicine's MRP will only be readjusted following an increase in annual	What is the justification for not allowing prices to rise as usage diminishes? Making this unidirectional suggests that it is a revenue	A working group should be formed to develop consensus on the details of

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			units sold. A patented medicine's MRP will not be readjusted following a decrease in annual units sold, or if its realized revenues fall into a lower tier.	control tool rather than a tool to assess and control for excessive prices.	application of the Guidelines on drugs for rare diseases.