Merck Canada Inc.

Response to Consultation Request – Patented Medicines Price Review Board

June 2020 Draft Guidelines

August 4th, 2020

Merck Canada Inc. (" Merck") participation in this consultation is not intended and should not be interpreted as supporting the amendments to the Regulations. Merck continues to have grave concerns about the practicality and legality of the amended Regulations, which are the subject of an ongoing legal challenge. Merck reserves the right to oppose any aspect of the Guidelines that exceeds the jurisdiction of the Board under the relevant legislation.

1. The Fundamental Concerns with the June 2020 Proposed Draft Guidelines

Despite the changes made by the Patented Medicines Price Review Board ("PMPRB") in this June 2020 version of the Guidelines, the pricing framework is still unworkable for new medicines and vaccines for the following two key reasons:

- **Excessive price reductions:** While thresholds have been raised and price floors have been introduced for Category I medicines, the new Guidelines will still lead to substantial price reductions for many of the most innovative therapeutics coming to Canada, particularly in the areas of oncology and rare diseases, which are areas of high unmet clinical need. Merck has obtained third party analysis suggesting that Category I products would capture and reflect almost 80% of the industry's revenues[1] (versus the two-thirds acknowledged by the PMPRB). A system that captures almost all an industry's future revenue stream within the high regulatory burden classification cannot reasonably be characterized as a 'risk-based' approach to regulation. When combining the regulated list price and the confidential price decreases, the most innovative medicines will often be subject to total price decreases of over 50%. This will most certainly negatively affect the industry's ability to launch products in Canada and invest in health research, including clinical trials.
- **Significant uncertainty:** The revised Guidelines are more complex and generate even more uncertainty than the previous version. Pharmaceutical companies, such as Merck, will have to navigate through a labyrinth of new complicated formulas and processes, with limited clarity on how they will be applied. Specifically, there is too much discretion afforded to the PMPRB staff in establishing price ceilings. For instance, PMPRB's staff will have the authority to determine the therapeutic criteria level that applies to new medicines, which is an aspect that will have major implications on the level of rebates required. As well, section 94 of the draft Guidelines provides total discretion to Board staff to apply the price tests they see fit in the context of investigations. Ultimately, if there is this much uncertainty on how to price Canadian products, it will be

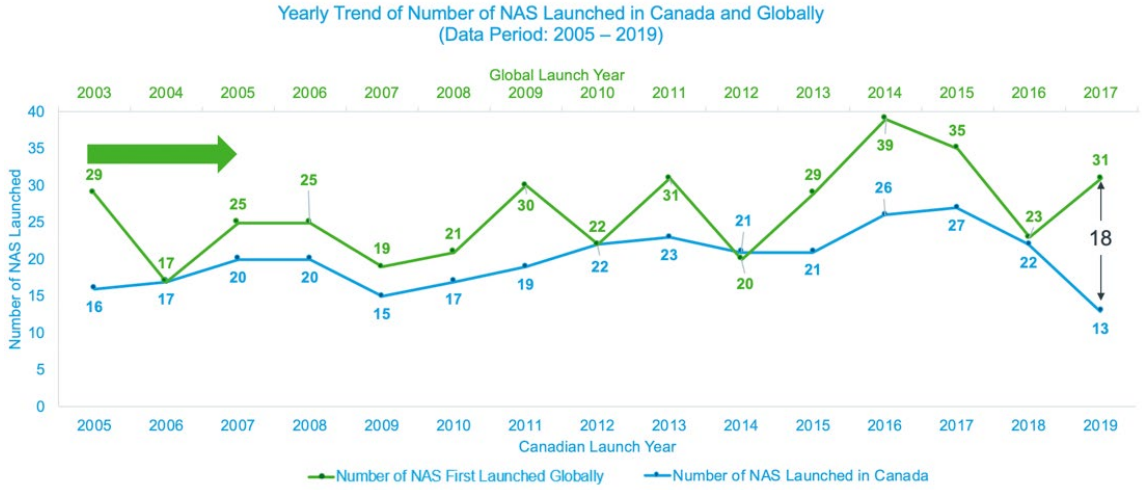
[1] PDCI assessment, data available upon request

difficult for Merck to make a compelling business case to its global headquarters to prioritize Canada for new medicine launches and clinical trials.

There is too much at stake to adopt the proposed flawed framework. At a time when new vaccines and medicines are needed to help combat COVID-19, we cannot afford to implement the untested new economic factors that would compromise Canadians' health. We should not be lowering prices of medicines at a level that will preclude patients from accessing new therapeutics to prevent or treat life-threatening or life-altering diseases. Specifically, even though COVID-19 medicines and vaccines are noted as being complaints based, they would still be subject to Category I and Category II conditions if investigated, as per PMPRB counsel clarification on the July 22nd, 2020 Vaccine Industry Committee teleconference.

<u>Early impacts from changing PMPRB regulations are already being felt</u>

Unfortunately, there is evidence that the new federal price controls have already reduced launches of new medicines in Canada and clinical trial activities. Specifically, according to recent data produced by IQVIA, a global leader in health data and analytics, there has been a sharp decline in the number of new drug launches in Canada in 2019. While Canada benefitted from 22 globally launched medicines (those that were launched in at least two major jurisdictions) in 2018, this number fell to just 13 in 2019 (see graphic below). Canada should have benefitted from closer to 30 launches last year.[2]

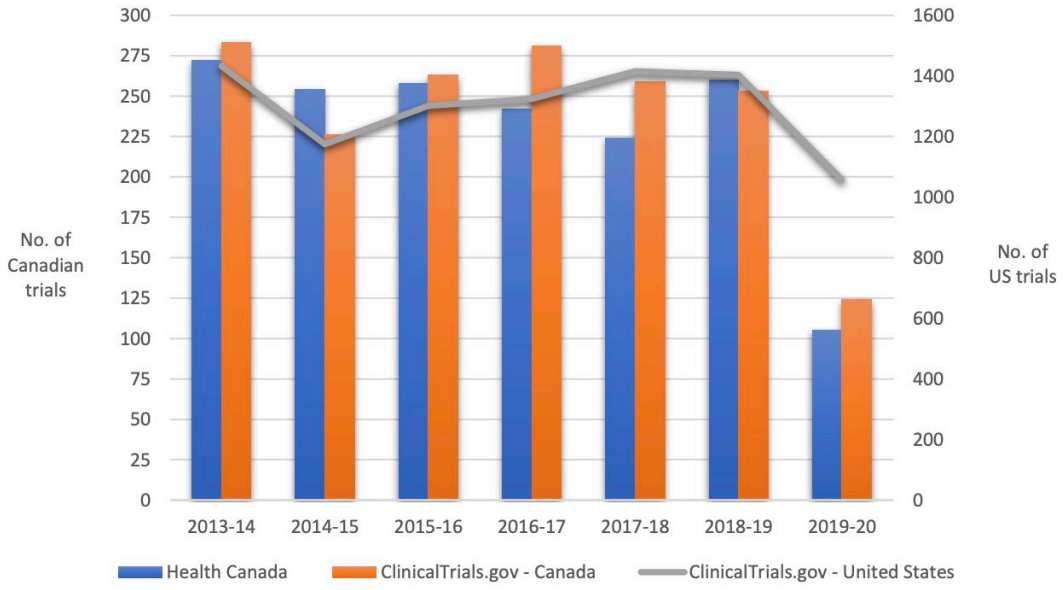


IQVIA MIDAS Database, all new launches within Jan 1, 2000 – Dec 31, 2019 (Data extracted on Mar 13, 2020). Top 25 countries based on 2019 sales. Austria and Sweden were excluded due to launch data quality. NAS: New active substance

[2] IQVIA Research, New Medicine Launches: Canada in a Global Context, June 2020, p. 13: https://lifesciencesontario.ca/wp-content/uploads/2020/06/EN_LSO_Global-Launch-Benchmarking_Webinar-June22-20_Final.pdf

In addition, according to another recent study, the number of clinical trials registered by Health Canada between November 2019 and mid-March 2020 fell by 52% compared to the average number registered during the same period in the previous six years (see Chart 1 below).[3] Of note, this drop in clinical trials occurred prior to COVID-19 hitting Canada, and much of this research includes high-cost, multi-centre clinical trials for cancer and other life-threatening diseases as opposed to minor studies such as Phase 1 studies and bio-availability and bio-equivalency trials that are aimed at generic medicines.

CHART 1: Numbers of clinical trials registered between November 1 and March 15, 2013-14 to 2019-20, Canada and the United States.



[3] Source: Nigel SB Rawson, PhD, *Canadian Health Policy*, April 2020, p. 4: https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada-decrease--a-sign-of-uncertainty-regarding-changes-to-the-pmprb-.html?buy_type=

Maximum rebated price ("MRP") cannot be implemented as drafted

The recent decision of the Federal Court of Canada makes it impossible for the PMPRB to apply the MRP component of the framework. The calculation of the MRP hinges on the disclosure of third-party, non-factory gate prices, which has been deemed to be *ultra vires* of the *Patent Act*. We are therefore extremely concerned by the PMPRB's July 8, 2020 statement indicating that it does not believe any substantive changes to the revised Guidelines are required as a result of this decision. This would appear to mean that the PMPRB is contemplating ways to enforce lower prices by circumventing the federal court's decision and/or by applying the new economic factors through a number of other regulatory levers, such as the following scenarios:

- The PMPRB insists on applying the 2020 draft Guidelines as-is, then patentees will have to meet very strict MRP targets without the benefit of the PLA rebates. Due to provincial restrictions on rebates to wholesalers and pharmacists, the only way to meet the MRP may be to literally give drugs away for free. And giving away substantial quantities of drugs for free can be problematic and could raise concerns of conduct that is "anti-competitive" in some contexts.

  Additionally, public and private insurers may likely still demand rebates, thereby further reducing the net sales and placing patentees in an impossible position. This will result in manufacturer's deciding to simply not launch in Canada.

- To avoid the foregoing, patentees may be forced to share the third-party, non-factory gate contracts with the board or face significant consequences. This would amount to the PMPRB doing indirectly what the Federal Court of Canada has stated the PMPRB cannot do directly.

- Moreover, due to the vast discretion afforded to the PMPRB in the context of their investigations, the Board may instead apply the pharmacoeconomic factors directly to the list price. This would entail manufacturers significantly dropping the list prices for Category I medicines and vaccines, which would have a devastating ripple effect on other markets. Since Canada is a reference country in other markets, prices in Canada also impact prices in other countries. This means that important transparent list price cuts in Canada could cause a chain reaction and hurt prices in other markets, which would discourage manufacturers from launching new medicines and vaccines in Canada. In sum, this approach would have an even greater negative impact on manufacturers' decisions to launch new medicines to Canada than the approach originally envisioned by the PMPRB when it first developed the MRP concept.

All these scenarios would have major implications for commercializing medicines and vaccines in Canada. Furthermore, any change to the application of the new economic factors would require the PMPRB to share with stakeholders updated Guidelines and a backgrounder outlining considerations, expected outcomes and operational and

administrative issues related to this major change. In other words, this would require additional opportunities for stakeholder input and discussion for the PMPRB to meet its obligation to consult with stakeholders found pursuant to section 96(5) of the *Patent Act*.

Additionally, Merck continues to be concerned with the way the PMPRB is proposing to apply the pharmacoeconomic factor and market size factor. Cost-effectiveness evaluations assessed by HTA bodies, in Canada and in other countries around the world, are used downstream in reimbursement decision-making. These analyses are meant to inform payers regarding value-based negotiations. It is inappropriate to use Canadian Agency for Drugs and Technologies in Health ("CADTH") or Institut National d'Excellence en Santé et Services Sociaux ("INESSS") evaluations for any purpose other than the intended objective of supporting reimbursement decision-making at the public drug plan level. Such analyses are subjective, and as such their outcomes fully depend on how various assumptions and input values are modified by reviewers during the assessment. As part of the negotiation process with payers globally, it is perfectly normal to seek a negotiated agreement that bridges the gap between the payer adjusted version of the assessment and the manufacturer version of the assessment. As a result, it is impossible for manufacturers to predict the outcome of a review, which underscores the inappropriateness of HTA as a rule for pricing.

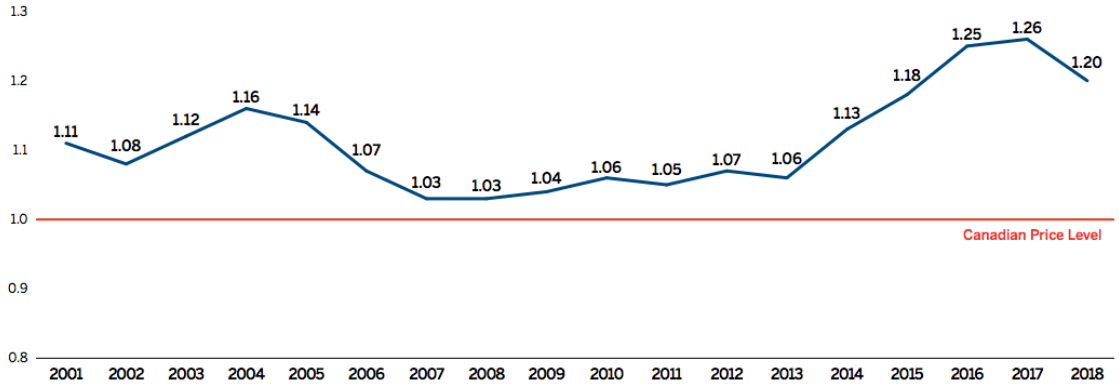
As well, PMPRB's proposed use of market size factor is completely disconnected from the notion of price excessiveness and amounts to a form of taxation or revenue control. This approach will end up unfairly penalizing companies bringing ground-breaking treatments to the market that address unmet medical needs and that could benefit a large number of patients. We continue to believe that market size is a more appropriate consideration for payers than for a price regulator, where the latter has the mandate of protecting consumers against excessive pricing of patented medicines. For instance, in the context of reimbursement, risk-sharing agreements are sometimes negotiated with payers under the pan-Canadian Pharmaceutical Alliance (pCPA) to address differences that can occur between forecasted and actual market size.

Given the negative impacts outlined above as well as the recent Federal Court of Canada decision, the routine use of the new economic factors, including pharmacoeconomic value and market size (e.g. as currently in the calculation of MRP), should be discontinued.

How far do Guidelines really need to go?

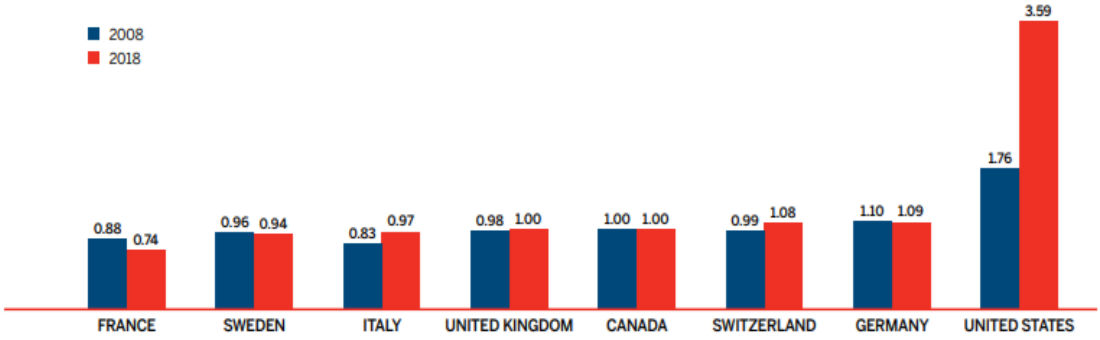
Implementing the modified list of countries alone would lower current drug prices for both public and private insurance plans. This price reduction is already substantive and on its own, is enough to achieve the savings originally contemplated by Health Canada at the outset of this reform (i.e. aligning with the middle of OECD countries). Through the application of the new economic factors, the PMPRB has overreached its mandate and gone well beyond Health Canada's initial objective. Further, it should also be underlined that the PMPRB's latest annual report shows that Canadian prices have consistently remained well below the median of prices found in the current basket of seven comparator countries (red line representing Canadian price level is always below international median, see Figure 26 below).

Figure 26. Average Ratio of Median International Price (MIP) to Canadian Price, at Market Exchange Rates, 2001 to 2018



Data source: PMPRB

Furthermore, as outlined in the PMPRB's 2018 annual report, Canada has remained at or extremely close to the median of the current PMPRB7 countries in 2008 (5th position) and 2018 (4th position). The pre-2019 Guidelines have clearly met the need to maintain Canada at the center of the basket of the 7 countries. It should also be noted from this annual report that spending on patented medicines decreased and overall prices also declined in 2018.[4]



Data source: PMPRB

Given the current COVID-19 pandemic, the PMPRB should be proceeding more cautiously and incrementally. This is not the time to be experimenting with completely new formulas, new concepts and new processes that have already discouraged commercialization of new medicines.

[4] PMPRB 2018 Annual Report, p.43 and p. 45: https://www.canada.ca/en/patented-medicine-prices-review/services/reports-studies/annual-report-2018.html

2. A New Path to Practical Guidelines

The following sections represent our commentary on how the PMPRB could consider improvements to maximize the practicality of the Guidelines.

Transitional Provisions

As previously outlined, no other industry in Canada has ever faced such material and immediate change to their revenue stream from the implementation of government regulations. Other regulations were progressively implemented to address burden of compliance, such as the changes to Canadian Food Labelling, in which the food industry had a transition period of 5 years to make these changes[5]. Similarly, after the "ratification of the Canada-European Union Comprehensive Economic and Trade Agreement (CETA) and the Comprehensive and Progressive Agreement for Trans-Pacific Partnership (CPTPP) [the federal government made] available $1.75 billion over eight years to Canada's nearly 11,000 dairy farmers"[6],

The industry would be much more able to comply with the implementation of the new Guidelines if there are provisions for bringing in the changes more slowly over time:

1. We will need to scale back some of our investments because of the lower revenues, and the Canadian third parties that rely on our company (i.e. supplier ecosystem, that include charities and other NGO's) would also need the time to adjust their operations. If pharmaceutical revenues are affected more slowly, the companies that depend on our funding, who tend to be principally local Canadian entities, will also be able to adjust their businesses to the changing reality.
2. Small and medium-sized Canadian based pharmaceutical enterprises do not benefit as much from global diversification of larger multinationals, and a sudden and rapid change in revenue could challenge their ability to maintain their operations.
3. All companies need time to adapt their business models to reflect the significant changes from the Guidelines. Some of the costs we need to adapt are linked to long-term commitments/contracts that would need to be re-negotiated.
4. In many of our customer contracts, there are triggering provisions linked to major market events. Major and rapid changes in pricing are more likely to

[5] https://www.canada.ca/en/health-canada/services/food-labelling-changes.html
[6] https://www.canada.ca/en/agriculture-agri-food/news/2019/08/government-of-canada-announces-compensation-for-supply-managed-dairy-producers.html

trigger the major market events clauses and would lead to several renegotiations versus having more time to deal with contracts as they come to renewal.

The current Guidelines has clarified that the timing of compliance on grandfathered products (products with DIN's issued before August 21st, 2019) and GAP products (products with DIN's issued and sales after August 21st, 2019 but before January 1st, 2021) would be able to comply to the maximum list price changes by December 31st, 2021.

These clarifications would appear to partly recognize our recommendation for transition provisions.

To complete the recommendation for transition provisions, for 2022 and subsequent years, we suggest that there be fixed maximum annual price reduction limits (e.g. no more than 5% negative list pricing impact per twelve-month period under the new Guidelines).

For example, the PMPRB could benchmark a required total level of price reduction and require patentees demonstrate a 5% price reduction to be verified at the end of 2022, and at the end of each subsequent reporting period, until the identified total price reduction requirement is met. This progressive implementation is fully aligned with the proposition made by our colleagues within the IMC submission.

<u>Guiding Principles in Development of the Next Draft Guidelines</u>

Merck fully anticipates that the PMPRB will need to change the June 2020 draft Guidelines based on the recent developments from the Federal Court judicial review, and without visibility to those changes at this time, we wish to re-iterate the four principles proposed earlier in 2020 which best balance ***feasibility, fairness, clarity, and predictability***.

1. ***Maximize Canada in the middle of the basket of 11 countries:*** The PMPRB specifically stated within the Guideline backgrounder in November 2019 that: "[we are seeking] prices of patented medicines in Canada that are more closely aligned with prices in like-minded countries"[7] and "[It is] Canada's responsibility to pay its fair share for global biopharmaceutical innovation"[8].

   Anything in the Guidelines that prioritizes pricing in Canada that is close to the international median of the comparator countries would be consistent with these statements. In contrast, any component of the Guidelines where the predominant

[7] https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/draft-guidelines/draft-guidelines-2019.html (page 3)
[8] https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/draft-guidelines/draft-guidelines-2019.html (page 13)

situation would lead Canada to being the lowest in the comparator group would not be consistent with this approach.

The most recent version of the Guidelines appears to best represent this principle by evaluating the maximum list price against the median of the basket of 11 countries. The elimination of the domestic therapeutic class comparison, protected by lowest international price, in this draft version of the Guidelines, further emphasizes the goal of maximizing Canada in the middle of the basket of 11 countries.

However, the inclusion of domestic therapeutic class comparator (dTCC) and international therapeutic class comparator (iTCC) in setting the interim manufacturer's list price ("iMLP") continues to elevate the risk that Canada will not be close to its peers, especially in a situation where Canada is one of the first countries to launch, and would specifically delay the launch of products. Clearly, this would not be beneficial for Canadian patients who want access to the latest innovations.

Guidelines that push the Canadian maximum list price well below its international peers risks delaying launches in Canada and even impeding launching altogether. Maintaining a fertile product launch environment in Canada, has the additional benefit of maximizing competition and the corresponding reduction in oversight burden for the PMPRB.

2. ***Utilize a Risk-Based Approach***: The PMPRB has stated on numerous occasions that there is an attempt to create a system where higher risk medications would have greater scrutiny, and lower risk medications would require less burdensome compliance[9]. There are clear cost considerations for the PMPRB and the industry in only focusing on products that present higher risk versus applying a heavy burden of monitoring on products that pose little to no risk to Canadians.

   This risk-based approach was already demonstrated with the reduction in reporting for generic medications and over the counter medications. Similarly, the automatic classification of generics and biosimilars as Category II demonstrates the usage of this principle.

   In contrast, allowing the classification of vaccines as Category I because of large market size, violates this principle. Vaccines are recognized as the most cost-effective intervention and procured by the federal government, provinces and

[9] https://www.canada.ca/en/patented-medicine-prices-review/services/consultations/draft-guidelines/draft-guidelines-2019.html (page 4)

territories through a highly developed tendering system. Spending on this health intervention is directly correlated to a public health benefit. The value of vaccines is being realized through the use of these entities combining not only competitive and negotiated prices but efficacy, effectiveness, security and predictability of supply. Therefore, the risk for such products is extremely low.

Similarly, products which have patents but are subject to generic competition represent an extremely low risk of patent abuse. A demonstration of the risk-based approach would be to classify the products with patents but subject to generic competition, under the same rules as the generics.

3. ***Balance the Consequences of Implementation:*** A balanced approach, in the context of the Guidelines, entails balancing the consequences of the implementation, versus only having reductive/negative consequences on pricing.

   For example, it would be consistent with a balanced approach if, in the presence of price ceilings, there would also be price floors. The PMPRB has demonstrated a version of this in the establishment of maximum price reduction for the market size economic factor and a maximum reduction for the pharmacoeconomic factors (for Category I medicines that are either high cost or have a high market share potential).

   It should be said, that beyond the mere presence of such floors, the quantitative value of such floors should be fair, especially considering the first principle above of maximizing Canada in the middle of the basket of 11 countries. Floors with 50% reductions, particularly when compounded by other aspects of the Guidelines, are excessive. This is especially punitive to innovative medicines that may at a later time after the introductory period produce new studies or a new relevant indication that show more clinically impactful improvement hence would warrant a higher MRP. Once product listing agreements are put in place to comply with the initial therapeutic criteria level, i.e. -50% level, it would be practically impossible to renegotiate agreements with payers to increase price. Less excessive floors would maintain a balance of fairness.

   Similarly, allowing an increase in maximum list price in the presence of the increasing median of the 11 comparator countries and not simply a reduction from a decreasing median of the 11 comparator countries, reflects the principle of balancing the approach.

   In contrast, the PMPRB has established a price reduction in Category I products from market size that can never go back up, even in the presence of heavy competition and loss of market share from this competition, which would also be inconsistent

with the second principle of utilizing a risk-based approach.

4. ***Create Bright Lines for Operationalization and Enhance Compliance Certainty:*** Guidelines without "bright line tests", would, "in the Board's opinion, not be in the best interest of the industry, the Board or the public. This approach would be expensive, time-consuming and confrontational rather than furthering the Board's objective of voluntary compliance"[10].

   There should be a careful equilibrium between the ability for companies to consistently meet the requirements of the Guidelines and the efforts required by the PMPRB to monitor/enforce compliance. Guidelines that are predictable, transparent, and that maximize objective rules versus requiring interpretation will enhance compliance certainty.

   The implementation of the highest of the therapeutic class comparison test, as per the current Guidelines meets this principle. However, using the median of therapeutic class comparators ("TCC") test in the establishment of the maximum rebated price, in the current draft Guidelines, is not a bright-line test. Patentees would systematically challenge the comparators in such a basket to obtain a more reasonable price. This would cause an unprecedented increase in resource use to settle disputes, investigations and hearings; much of which would be avoided by maintaining the bright-line highest of TCC test.

   Similarly, the classification of therapeutic criteria level (Level I-IV), which has similarities to the existing classification methodology (slight to no improvement, moderate improvement, substantial improvement and breakthrough), has been subject to many challenges[11]. There is a definitive risk of bias if the board staff is to make this determination. The stringent definitions proposed for the therapeutic criteria levels will most likely lead to most drugs being categorized as level III or IV. This is especially true for rare disease medications which typically get approved with immature, non-RCT data and could not, despite their clear clinical benefits, achieve the data requirements set out for therapeutic levels I and II.

   In addition, in reference to application of pricing tests for grandfathered products, using the NEAP would be operationally problematic given the complexity of the DIP methodology and the amount of back and forth required to resolve the differences. Much clearer is the usage of the actual current list prices that were considered

[10] Bulletin, Issue No.5; Patented Medicine Prices Review Board; December 1989 (page 3)

[11] These challenges led to the addition of the "moderate improvement" category in the 2010 Guideline update based on the Aderall XR hearing decision, Decision: PMPRB-06-D3-ADDERALL XR – Merits, April 10, 2008

compliant within the current Guidelines. The average transition price used in the NEAP has a degree of variation due to contracting variability (e.g. non renewed hospital contracts, lost tenders for vaccines). Using the existing list prices would represent a bright line test.

5. Conclusion

Clearly, one of the most problematic aspects of the Guidelines for Merck and the industry is the new economic factors and the way the PMPRB is proposing to apply them. The PMPRB has an unreasonably broad level of discretion to reassess a medicine and reapply the economic factors throughout the product life cycle. This will further drive pricing uncertainty, and this well beyond the excessive pricing standard, as an abuse of patent, reflected in the Patent Act. The recent results of the judicial review have significant implications for the operationalization of the maximum rebated price and there is an urgent need to address the required changes to these June 2020 draft Guidelines. Merck finds it extremely difficult to comment on, and to disentangle, a set of Guidelines that includes so many instructions on maximum rebated price.

If the PMPRB continues to proceed with the implementation of the Guidelines with the routine application of economic factors, Merck must explore all possible avenues to improve the Guidelines. Merck has outlined many practical challenges in complying with the Guidelines in their current form and proposed a balanced set of guiding principles that could be used to draft Guidelines that are feasible, fair, clear, and predictable.

Merck believes that the only way to work through these questions would be the implementation of technical working groups, particularly weighted on industry representatives that are responsible for the actual compliance activities and that have in-depth knowledge of the contracting environment in Canada. The concept of technical working groups has been utilized in the past by the PMPRB and once again, would provide the opportunity to generate practical solutions based on the realities of the pharmaceutical industry. As in 2011 and 2012, the legitimate consideration of the recommendations from the technical working groups is paramount to workable Guidelines.