



## **Merck Canada Inc. Submission**

Health Canada Consultation Paper *Protecting Canadians from Excessive Drug Prices  
Consulting on Proposed Amendments to the Patented Medicines Regulations*

June 28, 2017

## Executive Summary

The purpose of this document is to provide the views and recommendations of Merck Canada Inc. (Merck) on the Health Canada Consultation Paper, *Protecting Canadians from Excessive Drug Prices – Consulting on Proposed Amendments to the Patented Medicines Regulations*, released on May 16, 2017. Merck would like to thank Health Canada for the opportunity to provide feedback and look forward to participating in the public consultation looking at broader reform and consequences across the entire model in Canada for funding, sustainability, and delivery of healthcare as well as predictability of drug prices.

We would like to highlight our support of the submissions to Health Canada by Innovative Medicine Canada (IMC) and BIOTECanada (BTC). As we enter into this dialogue, it is important to note that the policy objective of the PMPRB to date has been largely achieved as Canadian prices for patented medicines remain below the international median. The regulatory proposals outlined in the consultation document are directional and high-level, with little explanation on potential impacts of specific regulatory changes and how they would be operationalized. Merck agrees with IMC and BTC that the policy issues and objectives for any proposed changes in the Consultation Paper should be supplemented by evidence, cost-benefit analysis and rationale as well as insights and perspectives brought to the policy discussion by all stakeholders.

At Merck, we are committed to innovation and investing in research – all with the purposes of helping people live better and longer. We strongly believe in the importance that medicines and vaccines play in helping people to live better while lowering overall costs in the health system. We are also very proud of our ability to bring clinical trials and related investments to Canada so that patients, clinicians, and hospitals can benefit.

In markets across the globe today, continuing budget pressures are motivating payers to make pricing and formulary decisions for innovative medicines based on the perceived affordability of new therapies, rather than primarily focusing on the value that the health technology provides. For our part, Merck is taking active steps in Canada and globally to demonstrate our commitment to responsible pricing and investing in the next generation of health solutions. We understand the need to improve the level of innovation and sustainability of the Canadian healthcare system. This includes improvements to the PMPRB, but not in isolation nor without thoughtful dialogue on policy rationale and operational impacts. Broader reform and consequences across to the entire model in Canada for funding, sustainability, and delivery of healthcare as well as predictability of drug prices should be considered. Reform must first and foremost prioritize patient impact.

Pricing of new innovative drugs in Canada should seek to strike a balance that ensures Canadian patients have timely access to new and beneficial medicines at a fair and reasonable price. As currently written, the proposed PMPRB regulations threaten to upset that balance and put Canada's future access to new innovative medicines at risk by shifting the focus from the current practice in Canada of price determination based on a new medicine's incremental therapeutic value to one where the list price of a new drug will be established largely by the government price regulator's assessment of affordability for public and private payers. This represents a radical departure from current practice, is untested, and is inconsistent with where most other countries are evolving their pricing practices toward value based contracting on clinical outcomes, economic risk sharing, and enhanced system efficiency between a drug manufacturer and a payer for a given patient population.

The PMPRB forms only one part of a complex system that governs the pricing and reimbursement of pharmaceutical products in Canada. New therapies are rigorously evaluated by health technology assessment bodies to ensure they are cost effective and provincial and federal governments work collectively via the pan Canadian Pharmaceutical Alliance (pCPA) to negotiate significant price reductions from the list price of a medication. This current practice is accountable to both broaden access and make drug benefits more sustainable. Therefore, these proposed reforms need to be considered in this broader context.

With regard to providing feedback on the proposed regulatory reform, it is difficult given the lack of clarity and assessments to date for the government's proposal. Specifically, we believe clarity of intent and additional information in several areas is absent in order to fully assess the implications of the proposed changes on patient access to new medicines and Merck's commercial operations in Canada.

- Canada leads the G7 in economic growth<sup>1</sup> and has the highest expected average growth from 2017-2021. It is unclear why the proposed regulatory changes seek to reduce revenues of an innovative healthcare industry by up to 25% as suggested by Minister Philpott in her speech of May 16th at the Economic Club of Canada<sup>2</sup>. This appears to be unprecedented in terms of regulating any industry, and dialogue of consequences of such drastic measures such as investments, employment, or product launches would further inform the discussion.
- Overall, Canadian prices have been below the international median on a consistent basis; falling to 18% below in 2015. The NPDUI report, *Drug Med Watch 2015*<sup>3</sup>, released by the PMPRB in April 2017, concluded that Canadian prices for New Active Substances (NAS) are 5th lowest of 7 countries. The Fifth Estate program in 2017, *"The High Cost of Pharmaceuticals: Canada's Drug Problem"*, made reference to Canadian generic medicines having some of the highest prices in the world. It appears that generic drug prices in Canada are consistently higher than international comparator countries; while patented drug prices are consistently lower. So, it is unclear in the consultation what component of drug medicines is creating the misperception of high prices of drugs in Canada.
- A country's pharmaceutical pricing and access policies are key factors that global companies consider when deciding where to direct investments. The proposed changes to the PMPRB may fundamentally affect Canada's attractiveness for global investment. Health Canada's proposals present a concrete risk that medicines will launch later in Canada. Should this occur, the evidence points to a risk that Canada will also have greater difficulty attracting clinical trials. Access to drugs through clinical trials is another way in which access is provided by pharmaceutical companies at no charge to the patients or the government.
- The consultation paper fails to acknowledge that the primary beneficiary of the proposed changes is the private insurance market. Government-sponsored drug plans already secure best value for innovative medicine prices via the pCPA. A net transfer of value to private drug plans risks making it more difficult for government-sponsored drugs plans to secure best value for the vulnerable populations they cover. Private payers in Canada have the mechanisms required to negotiate confidential agreements with our industry, if they so choose. We know of no other jurisdiction where for-profit private payers have successfully lobbied government to negotiate prices on their behalf.
- It is unclear how the regulatory changes support the Federal Innovation Agenda as a priority of the Federal Government and identifying "health and life sciences as one of the 6 sectors we are betting on for future growth, and investing in as part of the superclusters competition".<sup>4</sup>
- It is also unclear how the regulatory changes support the alignment of a parallel system for regulatory and health technology assessment review since as proposed there likely would be further delays, or no access, to new innovative medicines deemed to be the new standard of care.
- It is unclear how and under what circumstances the PMPRB will incorporate pharmacoeconomic evaluations, the size of market and GDP in Canada vs. comparator markets to inform price tests.
- Proposed changes to the PMPRB's pricing framework will introduce unnecessary costs to taxpayers/duplications/redundancies in the drug review system, which would delay patient access to new medicines. For instance, PE evaluations and budget impact analysis are already considered as part of other processes in the Canadian drug review system. Ultimately, drug affordability and pricing is appropriately addressed within the mandate of payers.

- It is unclear how the revised list of comparator countries was developed. Canada is different from all of the new proposed comparator countries. We have a mixed public/private system for pharmaceuticals. In some important ways, we are closer to the United States than most European countries in terms of how drugs are covered. The proposed countries for addition also have lower levels of access to new product launches according to the PMPRB's recent report on new medicines. Specifically as reported by PMPRB, Canada has access to 61% of new medicines introduced since 2009 while 5 of the 7 countries proposed for inclusion in the basket have levels at or lower than 45%.
- It is unclear why and how the PMPRB proposes to use and apply new information regarding discounts and rebates provided by manufacturers. We want to understand the purpose of requiring reporting of rebates and how the information would be used to establish a new products list price and the likely adverse consequences on price referencing of Canada by other countries.

**Merck Recommendation:**

Merck supports IMC's recommendation to partner with F/PT governments to develop a better approach for drug reimbursement and price regulation in Canada. We suggest that there be a **pause** in the process and reconsideration of the changes being proposed by Health Canada and hold substantive and meaningful consultations on the proposed changes with all stakeholders, including patient groups, clinicians and the pharmaceutical industry, while being open to find ways to achieve the goals behind this reform.

- Health Canada should not incorporate pharmacoeconomic analysis in regulation as an additional PMPRB excessive price determination factor. Furthermore, PMPRB should not use market size or GDP as factors given the inherent challenges. If these factors are adopted, Merck agrees with Innovative Medicines Canada recommendation that they should only be used in a secondary capacity, in the context of hearings or specific investigations, for products with no comparators and a high cost burden where the existing factors are insufficient to make a determination.
- Merck believes that Canada should seek to benchmark internationally against leading economies and health systems, as opposed to the OECD median. For any comparator country, the selection criteria and method of application should be coherent and transparent, and there are compelling reasons to retain the United States as a comparator country.
- Merck agrees with IMC and acknowledges that a relatively small number of patented medicines present a higher risk of excessive pricing, namely those with no comparators over the patent period. We propose that an Alternative Dispute Resolution (ADR) mechanism be formally established to aid the PMPRB in establishing price ceilings for medicines that have no comparators and a demonstrated high cost burden. An ADR mechanism for this select category of medicines would allow a "Drug Watch" period during which price ceilings could be negotiated by PMPRB staff and patentees without the cost, time and distraction of a formal quasi-judicial Hearing. Further, such a mechanism would address the risk this category of medicines poses in a targeted way, while avoiding the risk of broader negative unintended consequences for payers, patients and the life sciences cluster outlined above.
- Given the lack of information on purpose and use of Manufacturer provided confidential rebate information, potential legal concerns and the risk of unintended consequences for public payers and other market participants, Merck agrees with IMC recommendation that the government not proceed with making submission of indirect price reduction information to PMPRB mandatory for patentees.
- We agree with F/P/T governments that Canadians should have timely access to the medicines they need without affordability as a barrier. We are keen to engage with F/P/T governments, CADTH, INESSS and PMPRB build a predictable, stable and sustainable role for the innovative pharmaceutical industry and ensuring that Canadians continue to get value from their drug expenditures.

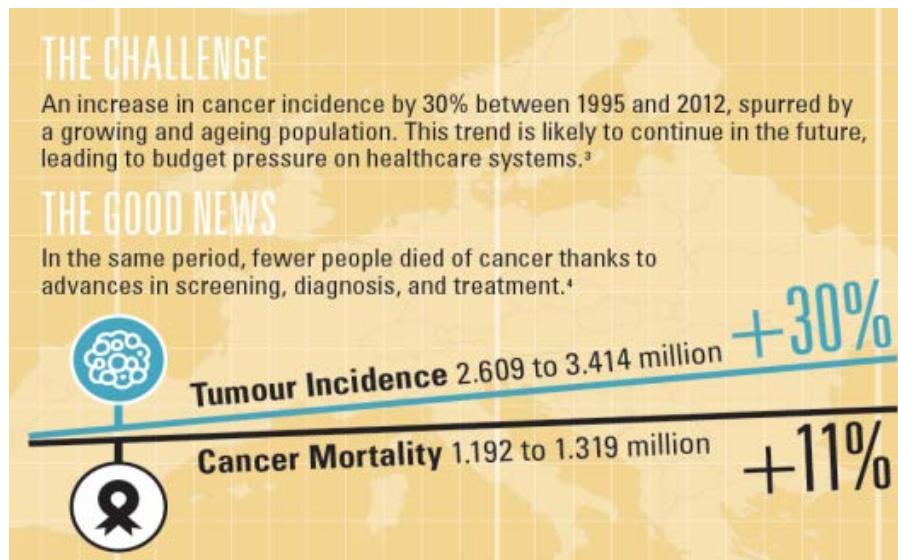
We look forward to continued engagement with Health Canada and the Board and other stakeholders during this very important discussion as the outcome of this consultation will have a significant impact on both patient access to innovative medicines and healthcare system sustainability.

## The “eco-system” for Pricing and Reimbursement Key Factors for Consideration

In our response, we first highlight key factors that must be considered in the consultation process and then address the specific issues outlined in the Consultation process.

Merck believes the Health Canada public consultation requires a common and balanced understanding of the current drug spending and pricing environment in Canada. The “eco-system” for pricing and reimbursement has evolved tremendously, both globally and within Canada, to ensure access to innovative medicines while managing drug spending and affordability of medicines. However, we understand the need to improve the level of innovation and sustainability of the Canadian healthcare system. This includes improvements to the PMPRB, but not in isolation. Changes to the entire model for funding and delivery of healthcare and different pathways to predictability and sustainability should be considered. This section provides key factors that must be considered in the consultation process and an overview of what is working well and potential area of improvement.

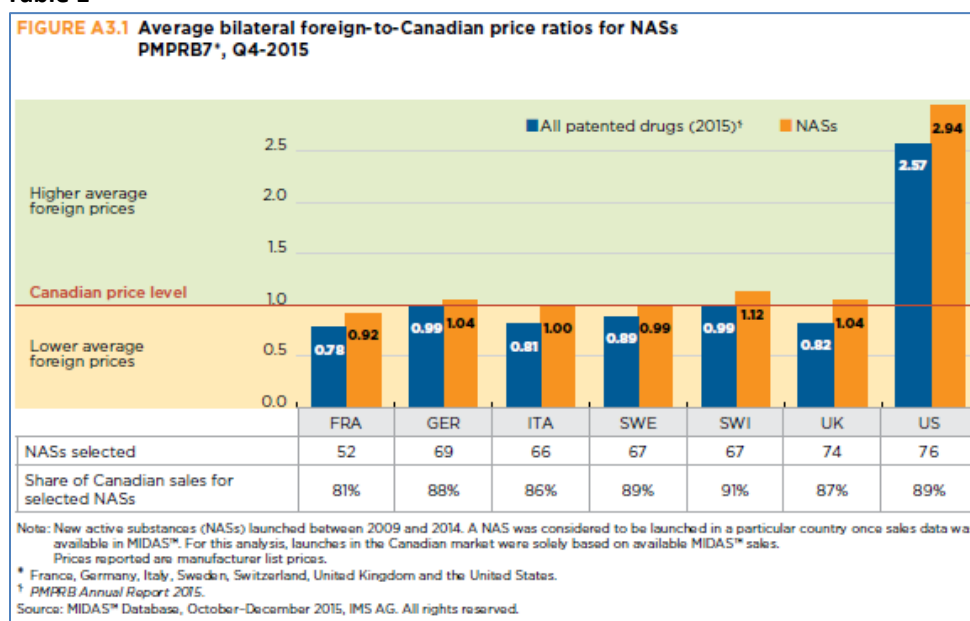
- **Value of Innovative Medicines:** Essential to a strong health care system in Canada is the rapid introduction and access to innovative medicines. Innovative medicines deliver great value for patients and society.
  - Millions of people worldwide are living longer, healthier, more productive lives today thanks, in part, to better healthcare and access to innovative medicines and vaccines.<sup>5</sup>
  - Medicines, for example, HIV/AIDS and Hepatitis C, can also benefit sustainability of the overall health care system and society by reducing hospitalizations and other costly complications of disease.<sup>6</sup>
  - A recent study conducted by the Conference Board of Canada found that the benefits of medicines offset the costs by a 2:1 ratio. These benefits included reduced productivity losses as people recover and return to work.<sup>7</sup>
  - Scientific development has resulted in new options to treat cancer which did not exist before, prolonging survival<sup>8</sup>



- **Pricing of Innovative Medicines:** Many factors go into the pricing of drugs, and every medicine is somewhat different, but in simple terms we consider the three core factors: the *Demand* in society, how well a medicine *Delivers*, and *Development*.

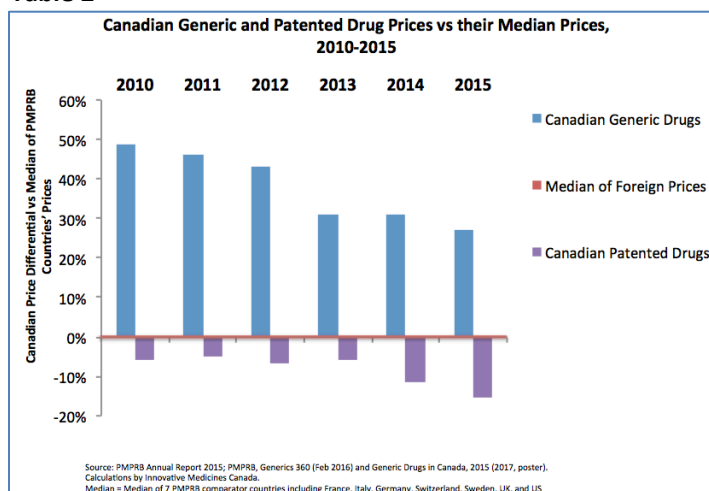
- *Demand* means we look at how well the drug meets critical needs in society and what treatments, if any, currently exist.
  - How well a medicine *delivers* means we look at the benefits of our drug, including how it can improve the lives of patients, and how it can prevent hospitalization or other costly complications of diseases.
  - And *development* means we need to price medicines to pay for ongoing research, discovery and clinical trials that will bring new treatments and cures.
- **Launch sequencing considerations:** Pricing in Canada impacts other countries, which reference Canada as part of a global pricing process including direct and indirect price referencing of Canadian list prices versus multiple international countries. This creates an important consideration for the launch sequencing of new innovations in Canada.
    - Historically, Canada has been a 1<sup>st</sup> wave country for new product introductions. Any changes to PMPRB Regulations & Guidelines must consider the impact on other areas of the eco-system and potential for unintended negative consequences that might impact launch sequencing (i.e. Canada becomes a 2<sup>nd</sup> or 3<sup>rd</sup> wave country).
  - **Canadian drug prices for new innovative medicines currently are in line with median foreign prices:** In the Consultation Paper, Figure A illustrates that Canadian patented drug prices are 3<sup>rd</sup> versus OECD countries. The methodology of the MIDAS IMS data base includes an average of all medicines (single-source innovative medicines and multi-source generic medicines).
    - However, international price comparison of single-source (no generic competition) patented medicines in Canada reveals that Canadian prices of single-source innovative medicines are 43% below the median international prices and its ranking in the PMPRB7 drops below the median.<sup>9</sup>
    - This finding was validated by an NPDUIS report, Drug Med Watch 2015<sup>10</sup>, released by the PMPRB in April 2017. This report identifies 210 new active substances (NASs) launched in Canada and in other International markets between January 1, 2009, and December 31, 2014, and analyzes their uptake, pricing, sales and availability as of the last quarter of 2015 (Q4-2015). The findings of this report conclude that Canadian prices for New Active Substances (NAS) are tied for 5<sup>th</sup> lowest of 7 comparator countries as illustrated in Table 1 below (orange bars).

**Table 1**



- **Canadian Drug Prices of Generic Medicines shown to be some of the highest in the world:** The Fifth Estate program in 2017, *“The High Cost of Pharmaceuticals: Canada’s Drug Problem”*, made reference to Canadian generic medicines having some of the highest prices in the world. <http://www.cbc.ca/news/health/health-minister-jane-philpott-drug-prices-1.3932254>
  - It appears that generic drug prices in Canada are consistently higher than the median among the PMPRB7 comparator countries; while patented drug prices are consistently lower<sup>11</sup> (Please see Table 2 below). So, it is unclear in the consultation what component of drug medicines is creating the misperception of high prices of drugs in Canada.
  - It is imperative that policy decisions on pricing regulation of innovative medicines correctly separate the drivers of pricing in Canada and not attribute the higher generic prices to the need for further drug regulation on new innovative medicines when they are demonstrated to be in line with current country comparators.

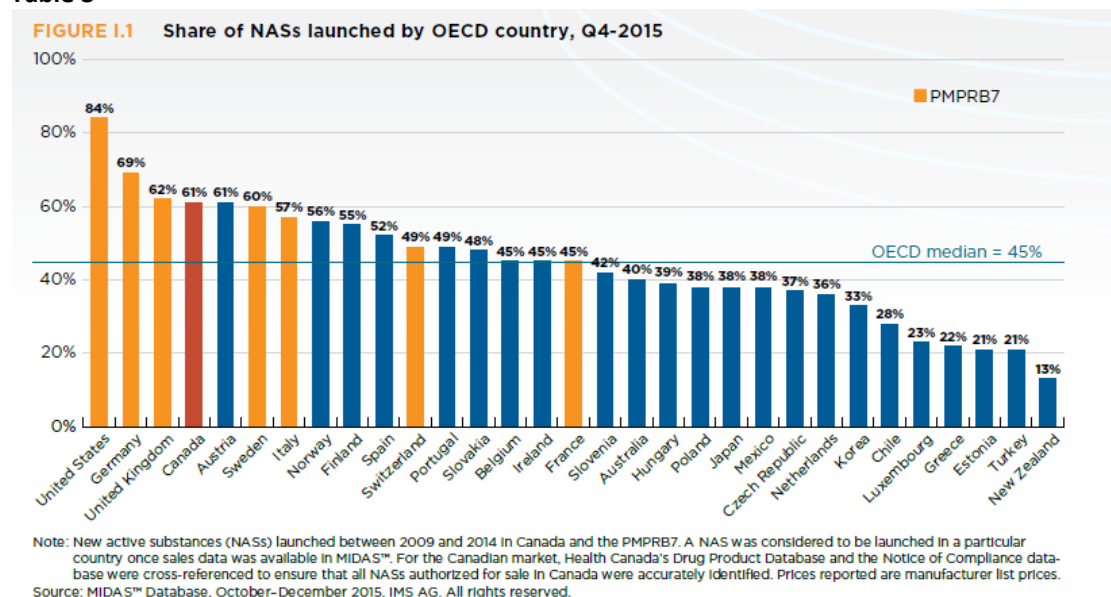
**Table 2**



Source: IMC review and calculations, 2017

- **Virtually all stakeholders agree that Canadians should strive for the best possible access to innovative medicines.**
  - Prices in Canada are reasonable and allow for Canada to be considered a top-tier country for new product launches by global manufacturers; hence enabling patients in Canada to have early access to these medications for optimal health outcomes.
  - As seen in Table 3 sourced from PMPRB’s NPDUIS Market Entry Watch 2015 Report of April 2017, Canada is the fourth highest country with access to 61% to new active substances launched. However, of concern is that 5 of the 7 countries being proposed for inclusion in the new international comparator market basket in the price regulations have access to less than the median for the OECD. This potential unintended consequence and the actual aspiration in Canada to improve, not reduce, access to new medicine should be part of the robust consultation sought at this time and not deferred to a later discussion on overall reimbursement pathway reform. A cost benefit analysis is warranted to determine whether a policy objective of reducing prices to price levels of the OECD median would translate to reduction of access levels in Canada to the OECD median.

Table 3



- **What is working well:**

- **Canada’s regulatory, reimbursement and pricing “ecosystem”:** There are many processes in place in Canada to ensure that innovative medicines are reasonably priced, and that Canadians are getting good value from these medicines.
  - ✓ Prices of new patented medicines are controlled in Canada through the federal government’s Patented Medicine Prices Review Board.
  - ✓ Additionally, all new therapies are rigorously evaluated by health technology assessment bodies to ensure they are cost effective and provincial and federal governments work collectively to negotiate significant price reductions from the list prices of medications.
  - ✓ *Going forward, it will be important that the role of the PMPRB and any subsequent modernization remain complementary and not duplicative nor overlapping with the role of payers and HTA contributors as it has potential to increase administrative hurdles to access to new innovative medicines in Canada and as well as duplicate functions already performed by other stakeholders.*
- **Differential pricing allows pharmaceutical companies to fulfill societal expectations to provide access to affordable drugs to all segments both locally and globally.** The development of innovative medicines requires significant investment to continue research and development. The established practice of differential pricing is critical as it distributes the burden of sustaining the capital investment required to fund medical innovation while at the same time ensuring the broadest access possible. *If price differentiation were replaced by a single global price, prices would tend to rise in less wealthy markets. This could present a financial barrier to access for the vulnerable populations in less economically developed countries.*

From a Canadian perspective, differential pricing has greatly contributed to enhanced access to innovative medicines and the sustainability of public drug benefits, and should be recognized by policy makers for healthcare in Canada as such. Publicly funded drug plans cover the majority of health care spending and provide access to medicines to the elderly as well as the most vulnerable populations. Providing differential pricing to public drug plans, therefore, is consistent with the practice by Canadian governments to ensure that those at greatest need are not penalized by their inability to pay. It also provides a solution to issues of affordability and



sustainability for all payers including, private payers, who have their own capability to work with innovative medicines companies to negotiate drug price to benefit their covered lives.

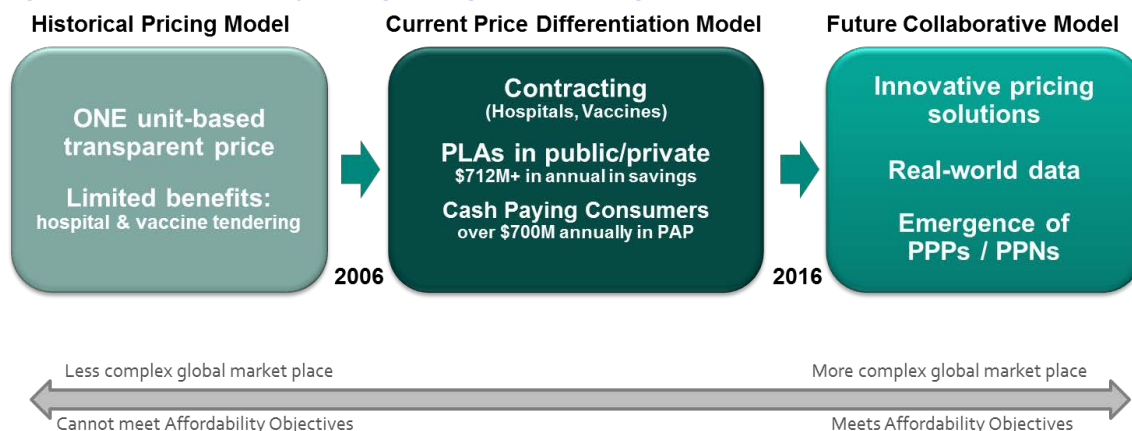
- **Confidentiality:** A critical factor in securing these savings is the ability of manufacturers to maintain the confidentiality of the financial terms. This confidentiality respects that the pharmaceutical market is global and that Canada is directly and indirectly referenced by international countries. Consequently, any policy initiatives to lower Canadian list prices below levels of international comparators could interfere with the ability of manufacturers to provide these greater savings, and therefore, put at risk Canada's position as one of the first-tier countries for launch of new medicines, which extends rapid access, and which would ultimately impede access to innovative medicines for consumers.
  - ✓ It should be noted that there are also potential legal issues with respect to whether the mandatory reporting of this information set out in this proposal could be ultra vires with respect to PMPRB's jurisdiction under the Patent Act, and/or with respect to the Federal Government's jurisdiction with respect to intellectual property under the Constitution Act, 1867.
  - ✓ Merck Canada strongly believes that this system of differential pricing supports the preferential targeting of resources to protect against an inability to pay. It is a key tool in supporting overall affordability of innovative medicines. Compromising the ability of manufacturers to offer these types of arrangements may negatively impact the ability of public plans to reimburse certain medications. Certainly, no analysis has been offered by Health Canada as to the market impacts including on overall launch sequence.
- **Patient Assistance Programs:** When patients lack coverage or cannot afford their out of pocket costs for our medicines in Canada, Merck offers programs to help, including our Patient Programs that have helped appropriate patients obtain the medicines they need through financial assistance or outright compassionate (free) product. Access to drugs through clinical trials is another way in which access is provided by pharmaceutical companies at no charge to the patients or the government.

- **Areas of Continued Improvement**

- **Sustainability:** Merck understands the importance of ensuring long-term health system sustainability and we want to do our part in helping achieve this goal:
  - ✓ We can optimize the use of therapies in areas of real unmet medical need such as cancer and heart disease, and infectious diseases like hepatitis C, HIV, Ebola and drug-resistant pathogens.
  - ✓ We are introducing personalized medicines, such as our immunotherapy treatments, can play a role in reducing healthcare costs by targeting patients who will most likely benefit from the treatments.
- We are also preparing to bring to market a diversified portfolio of biosimilar medicines in Canada over the coming years. Biosimilars can generate important savings for the healthcare system.<sup>12</sup> Despite the markedly lower price, the biosimilar market uptake has been modest in its first year of entry in Canada, estimated at 0.2% of the quantity of the molecule reimbursed by Canadian drug plans in 2015. Canadian payers would have benefited by an estimated \$41.7 million in additional savings if Canada had similar uptake as the OECD median.<sup>13</sup>
- **Fostering Innovation and for timely access to innovative medicines:** Merck supports the Federal Innovation Agenda as a priority of the Federal Government and identifying "health and life sciences as one the 6 sectors we are betting on for future growth, and investing in as part of the superclusters competition".<sup>14</sup>

- ✓ Merck supports using the platform of the Federal Innovation Agenda, outside of the PMPRB's mandate for regulating non-excessive drug pricing, as an opportunity to develop a forward-looking strategy for establishing appropriate goals and metrics for biotechnology and pharmaceutical innovation as an alternative to the outdated PMPRB approach to reporting of R&D spending.
  - ✓ Merck applauds the Health Minister for the initiative to improve timely patient access by prioritizing and streamlining processes of regulatory and health technology assessment reviews.
  - ✓ Health and industry policy are interrelated so proposed changes need assess the cost/benefit of providing an environment and timely access to medicines and quantify unintended consequences.
- **PMPRB Modernization reform needs to be aligned with the evolution of Payer drug pricing and not reversing back to practices of one transparent price for all payers that did not maximize patient access:** Figure 1 illustrates the progression of pricing practices in Canada. Initially, in a model where it was one transparent price for payers; then migrating to a model of product listing agreements with each jurisdiction to ensure patient access and greater payer affordability; this led to the pCPA negotiating on behalf of all F/P/T, which has been successful in securing consistent access at fair and affordable prices. Today, we observe pricing practices migrating into the 3<sup>rd</sup> box, i.e. collaborative innovative pricing solutions. For example, for eradication of Hepatitis C in Canada, collaboration between pCPA and manufacturers led to funding, competitive pricing that enabled broader access to innovative new medicines earlier in the disease progression. .

**Figure 1 - Evolution of Payer Drug Pricing & Contracting**



- ✓ What is being proposed within these regulatory changes is potentially replacing the current practice of list price setting on therapeutic value and confidential contracting for net price based on innovative pricing solutions with an new practice based on affordability and greater transparent pricing based on economic factors which is not only untested but in clear contrast with this pricing trends to date in Canada and in other countries.
- **Preserving a fair and predictable pricing and reimbursement environment within PMPRB Modernization:** As many manufacturers are subsidiaries or global organizations it is clear that the proposed changes to the PMPRB Guidelines need to adhere to principles of fairness and predictability in order to preserve a pricing and reimbursement environment that fosters innovation and timely access to the most appropriate innovative medicines for more consumers.

We acknowledge that a relatively small a number of patented medicines present a higher risk of excessive pricing, namely those with no comparators and some type of risk-based solution is required. Unless managed very carefully within the Guidelines, the addition of multiple additional factors may

result in additional investigations and hearings. From our point of view, this would not be a desirable outcome and would not result in a more risk-based system.

A better path forward would be that an Alternative Dispute Resolution (ADR) mechanism be formally established to aid the PMPRB in establishing price ceilings only for medicines that have no comparators and a demonstrated high cost burden. An ADR mechanism for this category of medicines would allow a “Drug Watch” period during which price ceilings could be negotiated by PMPRB staff and patentees without the cost, time and distraction of a formal quasi-judicial Hearing. Further, such a mechanism would specifically focus to address the risk this category of medicines poses in a targeted way, while avoiding the risk of negative unintended consequences for payers, patients and the life sciences cluster outlined above.

Merck believes that the proposals will not achieve the Government’s important policy objectives. Therefore, Merck supports a clearly defined, “bright line” PMPRB that is understood by all stakeholders. Given the multiple factors which influence the decision of whether to launch a given product and at what price point, we should collectively be looking to increase the level of predictability. We would support a regulatory approach that encourages patentees to launch products in Canada, to support robust market-based competition and the availability of options for payers across the system.

**It is critical in the cost/benefit analysis to understand how Health Canada predicts the prices of patented medicines to change as a result of these regulatory proposals and how these price changes will affect the Canadian pharmaceutical market and ultimately our health care system.**

## Regulation Changes

We would like to highlight our support of the submissions to the PMPRB by Innovative Medicine Canada (IMC) and BIOTECCanada (BTC). Merck agrees with IMC and BTC that the policy issues and objectives for any proposed regulatory changes in the Consultation Paper should be supplemented by evidence, cost-benefit analysis and rationale as well as insights and perspectives brought to the policy discussion by all stakeholders.

### I. Taking into consideration “willingness and ability-to-pay” of payers

#### Proposal

- Three new factors are proposed as criteria for PMPRB’s price evaluations:
  - **Pharmacoeconomic (P/E) evaluations:** The Board would require patentees to provide P/E information (similar to what they provide to health technology assessment bodies) along with budget impact analyses. The discussion paper reviews potential cost per Quality Adjusted Life Year (QALY) and affordability threshold calculations, noting that prices “could” be expected to fall within pre-determined threshold levels.
  - **Size of market:** The PMPRB would also be permitted to consider the size of the potential market for the drug and the product would be evaluated against certain market impact tests.
  - **Gross Domestic Product in Canada:** The impact on national and per capita gross domestic products would be considered in the context of excessive price evaluations.

#### Merck Perspectives

##### Pharmacoeconomic Evaluation:

An economic evaluation is defined as “the comparative analysis of alternative courses of action in terms of both their costs and their consequences”.<sup>15</sup> Cost-effectiveness (or “value” for money spent on treatment services) is of central concern in most health care and government systems. Economic evaluation is one of the tools available to help choose wisely from a range of alternatives and implement efficient resources.<sup>16</sup> Health economic evaluations are conducted to inform health care resource allocation.<sup>17</sup> As such, we do not agree that a pharmacoeconomic evaluation is appropriate to determine if the price of a drug is excessive. Rather, it helps decision-makers evaluate if the price of a drug is worth paying.

In Canada, pharmacoeconomic analyses represent one among many considerations in value assessments for informing drug funding decisions. Patient perspective, burden of illness, feasibility of adoption, and equity considerations are other criteria that are considered alongside cost-effectiveness when reimbursement decisions are made. The PMPRB is not a payer, and thus should not employ QALYs nor establish cost per QALY thresholds across the system to inform their pricing decisions.

Moreover, it is scientifically invalid to compare pharmacoeconomic evaluations across countries:

- Pharmacoeconomic analyses are context dependent; cost structures are different in other countries, so what is cost-effective in a given country may not be in another.
- For the same reason, ICERs will differ, and an acceptable ICER level will differ from country to country due to variations in other value factors (as described above).
- Thresholds are also context-specific and should not be imported. It also is important to point out that CADTH does not officially specify an ICER threshold for pharmacoeconomic evaluations in Canada.

Not only does Merck feel this factor is inappropriate, but we also challenge how it could be implemented in Canada. More precisely, we foresee the following specific issues with this proposal:

- Models submitted to CADTH and/or INESSS are of variable degrees of robustness and quality, due to choices of structure and/or underlying assumptions, for example. It is the HTA agencies' role to evaluate, critique, and modify the models. To do so, they rely on a number of highly trained experts in various fields such as modeling, statistics, epidemiology, and even specific therapeutic areas. The proposal would either result in inefficient duplication of work by the PMPRB, or in a suboptimal quality of evaluation of the pharmacoeconomic models.
- Considering cost-effectiveness analyses to regulate maximal allowable prices would introduce a level of uncertainty with regards to the MAP that may be unsustainable for industry. That uncertainty would be due to the fact that manufacturers could not use their models, as submitted to CADTH, to predict the MAP *a priori* because of the unknown modifications that will undoubtedly be performed by the reviewing agency. Industrial economics have demonstrated the uncertainty leads to under investment.<sup>18</sup>
- The CADTH Guidelines for the Economic Evaluation of Health Technologies: Canada (4th Edition) state that stratified analyses of subgroups should be conducted when factors that may lead to different estimates in costs or outcomes are identified. Moreover, the guidelines emphasize that probabilistic analyses should be performed. In practice, CADTH is moving away from the single incremental cost-effectiveness ratio (ICER) in order to evaluate drugs. Instead, CADTH is looking for the probability of a drug to be cost-effective in different patient populations, under various thresholds. It is unclear how PMPRB would utilize such complex analyses, adopting the public payer perspective only, to regulate prices for all Canadians.
- The assessment of value in the public market does not reflect value assessments within the private market because patients, families, and employers have different health objectives, tolerance levels for uncertainty, and willingness-to-pay. For example, employers are interested in promoting a healthy and productive workforce and reducing absenteeism. Given that the population covered by public plans and private plans differ, their value assessments will also differ. A single representative cost-effectiveness threshold cannot therefore be used to assess value of medicine for all Canadians.
- Willingness-to-pay relates to an individual's absolute value of an intervention based on their preferences. QALYs however do not fully represent an individual's preferences.<sup>19</sup> QALYs have been shown not to capture all dimensions of health benefits.<sup>20</sup> Analyses that rely on QALY comparisons will inherently favour therapies that have overall survival data available and will bias older agents versus newer agents that do not have the same level of data available.
- Analyses using QALYs also bias against comparisons to older generic drugs where prices have dramatically decreased (e.g. oncology, diabetes), and against conditions where there are many costs associated with surviving patients. For example, in some recent oncology models, even if the drug was priced as \$0, the ICER would still not be in the threshold range for some HTA bodies as patients surviving still require many medical treatments and costs (lifetime horizon).
- QALYs do not appropriately measure interventions that reduce short term-disabilities and/or many undesirable health states and difficult conditions for patients (e.g. nausea, vomiting, pain associated with use of contrast agents, postoperative recovery, etc.).
- A QALY framework has been demonstrated to present risks that the clinical benefits of interventions for a pediatric population will be underestimated, will result in artificially high ICERs, and could adversely impact innovation and the number of products to come to market for children.<sup>21</sup> Similarly, ICERs are not a relevant metric for drugs for palliative care and rare diseases. Most of the orphan drugs appraised to date have cost-effectiveness thresholds well above the 'accepted' level and would not be reimbursed according to conventional criteria.<sup>22</sup> If conventional cost-effectiveness thresholds cannot be met by such therapies, they still in most part do not hinder the affordability questions, as the patient group that uses such therapies may be very small and may not impact payer budgets.

This proposal could have several unintended consequences.

- By introducing uncertainty with respect to achievable MAP, it may cause manufacturers to rethink their launch sequencing for new products. Canada is a relatively small market in the global pharmaceutical world, yet it is a pricing reference for multiple other jurisdictions that, together, represent a bigger business opportunity. This could significantly delay access to innovative medicines for Canadian patients.
- The introduction of additional uncertainty in any industrial field has also been shown to lead to sub-optimal investment levels.
- Fixed cost per QALY thresholds for determination of non-excessive list prices could also have impacts on the availability of some drugs: it may not always make sense to launch in Canada if the MAP price is low relative to the business potential that this country represents.
- Fixed cost per QALY thresholds also create equity issues for patients with rare conditions and for certain patient subpopulations, e.g. children. Cost-utility analysis is poorly suited to drugs for rare disease where there are often evidence gaps due to small patient populations.

***As such, we believe that Health Canada should not incorporate pharmacoeconomic analysis in regulations as an additional factor to determine list prices. PMPRB is not a payer and, as such, should not consider ability-to-pay when determining the maximum allowable price. If a drug is not priced within the payer's affordability parameters, then the payer has the right to reject the treatment at the price offered, or to engage in dialogue with the treatment innovator to arrive at a mutual solution to affordability concerns.***

***There are several options available to payers:***

- ***restricted indication: limits prescribing to patients who will benefit most from the treatment; this reduces the size of the market and thus the budget impact of the treatment***
- ***price negotiation and innovative pricing solutions: a traditional way of resolving discrepancies between treatment value and affordability***
- ***managed entry agreement: pay for performance contracts which ensure resources are used only where health gain is realized***
- ***financing options: long-term financing /amortization of drug costs which allow access to medicines while maintaining short-term affordability imperatives.***

Market Size:

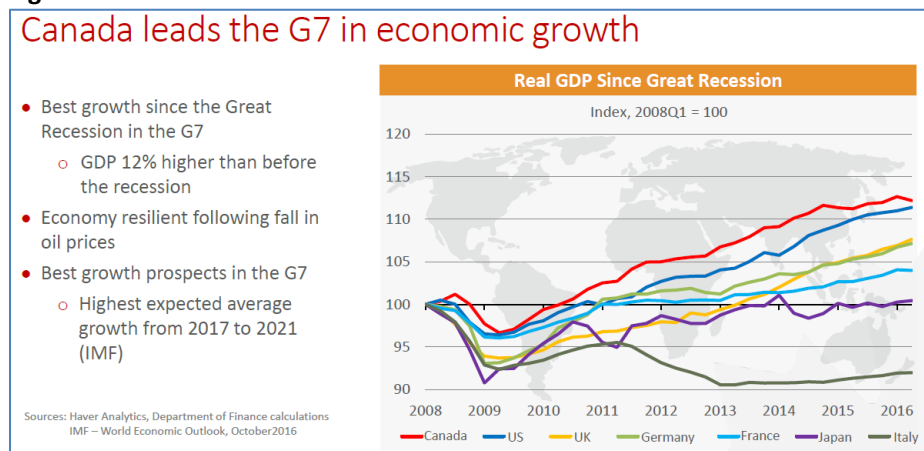
- It is unclear how the PMPRB will incorporate issues related to the size of market in Canada and in other countries to determine if prices are excessive.
- Not only is collecting and analyzing market size information from other countries a complicated process, but comparisons are also difficult to make given differences in product approvals, sequence and number of indications, monograph content, and labeling.
- With regards to considering the evolving size of the market in Canada to regulate prices, it is important to note that there are multiple explanations as to why the initial forecast and the actual performance may differ. This is why various forms of risk-sharing agreements currently occur downstream with individual payors, via pCPA negotiations for example. We therefore believe that market size is a more appropriate consideration for payers than for a price regulator.
- Besides focusing only on the price of drugs, an evaluation on how novel medications lower the overall cost of health care (reduced hospitalizations, surgeries, etc) should also be evaluated.
- Individual provinces and health plans will have a better mechanism to evaluate the true affordability question with respect to medications. They could employ several techniques (price/volume agreements, risk sharing agreements, pay for performance agreements, rebates/discounts, etc) that may not be effectively addressed through a national program. Such provincial and local actions not only help providing patients with access to innovative medications, but if necessary can also manage budgetary pressures.

***PMPRB should not use market size as a factor given the inherent challenges with the widespread application of market size factors for the purposes of assessing whether a given price may or may not be excessive. If this factor is adopted nonetheless, Merck recommends that it should only be used in a secondary capacity, in the context of hearings or specific investigations, for products with no comparators and a high cost burden where the existing factors are insufficient to make a determination.***

GDP and GDP growth:

- ✓ In terms of the proposed changes, since 2008, Canada leads the G7 in economic growth<sup>23</sup> and has the highest expected average growth from 2017-2021 (please see Figure 2) so it would be reasonable from a pricing perspective to maintain the level of fair prices that Canadians are paying today. The policy objective that Health Canada is trying to achieve with PMPRB modernization is unclear. Rather than aiming to reduce prices of innovative medicines in isolation, more focus should be placed on broader reform and consequences across to the entire model in Canada for funding and delivery of healthcare as well as predictability of drug prices and sustainability should be considered. High emphasis should be to fuel Canada’s economic growth with prioritization on the Federal Innovation Agenda with “health and life sciences as one the 6 sectors we are betting on for future growth, and investing in as part of the superclusters competition”.<sup>24</sup>

**Figure 2**



- We are unsure how to reconcile the note GDP growth trends with the fact that the Consultation Document proposes changes to the fixed basket of international comparator jurisdictions that includes countries with GDP levels below that of Canada. Additionally, it is unclear how and when this factor would be applied when there is the potential for other factors to be available to the PMPRB in the future that will not align with this proposed measure of GDP. It is also unclear when and how this factor would be applied against the other factors employed by PMPRB overall. Finally, it is also unclear whether and how this factor would impact price changes over time, for example, in cases where GDP increases or decreases by larger amounts between comparator countries.

***Recommendation: Given the outstanding questions related to how GDP and GDP growth may be applied by PMPRB, Merck recommends against its adoption. If this factor is adopted nonetheless, Merck recommends that it should this factor be used only in a secondary capacity, for example for the purposes of hearings or specific investigations, for products with no comparators and a high cost burden where the existing factors are insufficient to make a determination with respect to a specific product.***

### **Questions to inform consultations**

- What is the policy gap that Health Canada aims to address in applying new pharmacoeconomic analysis and affordability criteria to the PMPRB price tests?
- Has Health Canada considered the extent that this is a duplication of evaluations, which could delay or negatively impact access?
- What are the potential impacts of using the QALY and affordability thresholds, given their drawbacks and limitations (subjectivity, context-driven, etc.)?
- Under what circumstances would these new factors be used and how would the new criteria work in the context of current price tests, which prioritize therapeutic benefit and level of innovation as criteria?
- How will the new criteria impact timing and prices for the launch of new medicines in Canada?

## **II. Amending the list of countries used for international price comparisons**

### **Proposal:**

- The PMPRB proposes to remove two countries (the United States and Switzerland) from the current seven and add seven new countries (Australia, Belgium, Japan, the Netherlands, Norway, South Korea and Spain). Germany, the UK, Sweden, France and Italy would remain.

### **Merck Perspectives**

- The consultation document offers no insight on how comparator country prices will impact price reviews and be operationalized.
- Currently, prices in the PMPRB7 are used to set a highest price ceiling based on the highest list price in the basket over the life cycle. As well, the median price of the market basket has been a target at introduction. Since 1993, PMPRB has stated the policy objective that Canadian prices, on average, should not exceed the median of international prices in the PMPRB7. In 2015, Canadian prices declined to 18% below the median of the PMPRB7.
- It is unclear how Health Canada developed the revised list of comparator countries. Factors that may have come into play include per-capita GDP, ranking within the OECD group of developed countries, healthcare models, access to funded medicines within public and private health systems, availability of pricing data, R&D expenditure, etc. Comparators should reflect both the economic power of named countries in addition to their public policy objectives for market launches and patient access. In addition, the economic ties between Canada and the comparator countries should also be considered.
- However, Canada is different from all of the new proposed comparator countries. Importantly, we have two major payer types – public and private – both reimbursing and supporting access to innovative medicines in Canada. In some important ways, we are closer to the United States than most European countries in terms of how drugs are covered.
- There are many similarities between the markets in the United States and Canada: both are mixed private/publicly funded systems with multiple payers, and utilization and prescribing patterns are comparable. Geographic proximity and an extensive economic relationship (e.g. 70% of Canadian exports are to the United States, making it by far our most important trading partner) support a high degree of scientific and clinical integration and patient movement.
- The OECD list of 30+ countries contains a wide range of GDP per capita, R&D infrastructure and health system quality, access and expenditure. The OECD median became does not appropriately reflect Canada's global leadership position. Merck is aware of no other economic sector where Canadian prices or other regulatory objectives are linked to middle or average of the OECD.
- Canada should aspire and be compared to high performing systems. Canada leads the G7 in economic growth based on a report from the IMF so it would be reasonable and fair from a pricing perspective



that Canada continues to reference these wealthier countries including the United States. Differential pricing takes into account the value that medicines create in a given market as well as a particular health system's ability to pay for them. The practice recognizes that more developed, prosperous nations pay higher prices for innovation because it delivers more health economic value in these environments. The federal government has set aspirational goals seeking to place Canada in a global leadership position, frequently comparing Canada favorably to the world's largest and most powerful economies. Canada should not aspire to benchmark their health system to countries like South Korea and New Zealand.

- The proposed countries for addition also have slower access to new product launches according to the PMPRB's recent report on new medicines. In a graphic in that report, Canada is listed as having access to 61% of the new medicines being studied, which is the fourth highest in the OECD. The countries that are proposed for addition (Australia (40%), Belgium (45%), Japan (38%), the Netherlands (39%), Norway (56%), South Korea (33%) and Spain (52%)) have poorer access.<sup>1</sup> (Please refer to Table 1)
- In addition, Canada's list prices are currently referenced in 23 other global markets. Additional uncertainty regarding PMPRB non-excessive prices in Canada could have an impact on when a product is launched here.
- Acceptance of any new technology is dependent upon its adoption by the most affluent purchasers. It is unclear if the objective of linking Canada's pharmaceutical price ceiling to the OECD median is consistent with the Government of Canada's objectives to play a leadership role in the global context, and seems inconsistent with Health Canada's recently announced policy objective to accelerate the introduction of new innovative medicines into the Canadian market.

***Recommendation: Merck believes that any new grouping must acknowledge that Canada is at the forefront of the 35 OECD countries. Canada should seek to benchmark internationally against leading economies and health systems, as opposed to the OECD median. For any comparator country, the selection criteria and method of application should be coherent and transparent, and there are compelling reasons to retain the United States as a comparator country.***

#### **Questions to inform consultations**

- The criteria for choosing appropriate comparator countries in the consultation document are consumer protection, economic standing and pharmaceutical market characteristics. Are these the best criteria? Should we consider health outcomes, speed and quality of access to pharmaceuticals and other factors?
- If timeliness and quality of access are important factors, the countries that Health Canada proposes to add have poor track records with respect to speed and range of new therapies that are reimbursed. What can Canada do to preserve and improve timely, high quality and broader coverage and avoid lower access levels as observed in the countries being added as comparators?
- Will the median list price of the new comparator countries be the target? What level does the government propose to achieve? As noted in the recent PMPRB/NPDUIS report cited above, Canada's prices are already at or below the median.
- Are there other areas for drug expenditure reductions that do not risk reducing access to innovative medicines? For example, Canada could consider the increased use of generics and biosimilars and measures to achieve lower generic prices to bring Canada in line with comparator countries.
- Will reduced list prices lead to net savings by payers? If so, how will these savings be channeled into other health priorities and how will those priorities be determined?

---

<sup>1</sup> <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1307>

- What are the impacts of removing the United States from the list of comparator countries? Are there international trade issues? Could there be impacts on cross-border trade and sales in pharmaceuticals that could lead to drug shortages?

### III. Providing information related to third party rebates

#### Merck perspectives

- Although the proposals in the consultation document claim that the reported rebates will be kept confidential, it is unclear how the PMPRB would use and apply new information regarding net prices.
- If they are used to lower the transparent list prices to the benefit of private payers, it could impact the capacity for ongoing value and rebates to public payers in the context of listing agreements. There may be a misconception by public payers that lower list prices would lead to maintaining or even further lowering of net prices.
- Customer-focused pricing (i.e., differential pricing) achieves several important benefits that were unavailable in Canada prior to the availability of product listing agreements. Specifically, confidential transaction prices:
  - help payers achieve more value than transparent pricing, leading to more room to invest in a broader range of therapies within restricted budgets
  - substantial increase access to medicines for patients
  - provide flexibility to manufacturers that have to determine prices in Canada within the global context (Canada's prices are used to benchmark prices in 23 other countries)
- These benefits may be at risk if the PMPRB requires that all discounts be reported.

***Recommendations: Given the lack of information on purpose and use of the information, potential legal concerns and the risk of unintended consequences for public payers and other market participants Merck recommends that the government not proceed with making submission of indirect price reduction information to PMPRB mandatory for patentees.***

#### Questions to inform consultations

- If the PMPRB's mandate is to prevent excessive prices (i.e., an upper boundary), what is the purpose of requiring reporting of rebates and discounts? How will that information be used?
- Has Health Canada considered the potential operational, economic and health system impacts of mandated reporting of discounts and rebates?
- How does Health Canada propose to ensure PMPRB's compliance with the *Patent Act* and keep this information confidential?
- Do the provinces support this proposal, as they will have to grant the PMPRB the authority to collect most of this data?
- If public drug plans have confidential agreements that offer rebates, has Health Canada considered whether how and whether a reduction in list prices could impact savings for these governments and timely access to innovative medicines?

- 
- <sup>1</sup> The Canada Opportunity, The Economy and the Growth Agenda; Government of Canada. November 2016  
[http://www.international.gc.ca/investors-investisseurs/assets/pdfs/download/The\\_Canadian\\_Opportunity.pdf](http://www.international.gc.ca/investors-investisseurs/assets/pdfs/download/The_Canadian_Opportunity.pdf)
- <sup>2</sup> Minister Philpott in her speech of May 16th at the Economic Club of Canada: [https://www.canada.ca/en/health-canada/news/2017/05/economic\\_club\\_ofcanada-may162017.html?undefined&wbdisable=true](https://www.canada.ca/en/health-canada/news/2017/05/economic_club_ofcanada-may162017.html?undefined&wbdisable=true)
- <sup>3</sup> Meds Entry Watch, 2015; NPDUI: Patented Medicine Prices Review Board, April 2017
- <sup>4</sup> Minister Philpott in her speech of May 16th at the Economic Club of Canada: [https://www.canada.ca/en/health-canada/news/2017/05/economic\\_club\\_ofcanada-may162017.html?undefined&wbdisable=true](https://www.canada.ca/en/health-canada/news/2017/05/economic_club_ofcanada-may162017.html?undefined&wbdisable=true)
- <sup>5</sup> Lichtenberg F.R., *Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009*, NBER Working Paper No. 18235, July 2012. In this study, Lichtenberg found that life expectancy at all ages and survival rates above age 25 increased faster in countries using newer drugs.
- <sup>6</sup> See IMS Institute for Healthcare Informatics, “*Global Outlook for Medicines Through 2018*”, Parsippany (NJ): IMS Health Inc., November 2014. This is an updated global forecast for the use of medicines through 2018 that notes that much of the increase in global spending on medicines is expected to be attributable to medicines “*bringing new treatment options to patients, including breakthrough therapies or even cures that often reduce complications or hospitalizations while improving outcomes.*” See also “*Decline in Economic Returns from New Drugs Raises Questions about Sustaining Innovation*”, Health Affairs, 34, no.2 (2015): 245-252. This study states that, despite rising pharmaceutical costs to the U.S. health care system, pharmaceutical spending has frequently offset costs in other areas and suggests that additional cost containment measures could negatively impact future innovation. Specifically, it states that “*in 2012 the Congressional Budget Office began incorporating medical savings associated with the increased use of medicines among Medicare beneficiaries into its scoring estimates for federal health spending. This and other recent evidence suggests that better use of medicines can lead to lower health costs overall, and raises questions about the potential impacts on investment if drugs become the particular focus of additional cost containment measures.*”
- <sup>7</sup> *Reducing the Health Care and Societal Costs of Disease: The Role of Pharmaceuticals*, Conference Board of Canada, 2013.
- <sup>8</sup> MSD Infographic 2017; based on: Jönsson B et al. (2016), Comparator Report on Patient Access to Cancer Medicines in Europe Revisited
- <sup>9</sup> Form 2 Block 5 data submitted to PMPRB, July-December 2015, Innovative Medicines Canada members. Converted to Canadian dollars using PMPRB’s 36-month exchange rate ending December 2015
- <sup>10</sup> Meds Entry Watch, 2015; NPDUI: Patented Medicine Prices Review Board, April 2017
- <sup>11</sup> Innovative Medicines Canada (IMC) review and calculations, 2017
- <sup>12</sup> *Merck Canada News Release*, December 2015.
- <sup>13</sup> Market Intelligence Report. 1st Edition: Biologic Response Modifier Agents, 2015; NPDUI: Patented Medicine Prices Review Board, October 2016
- <sup>14</sup> Minister Philpott in her speech of May 16th at the Economic Club of Canada: [https://www.canada.ca/en/health-canada/news/2017/05/economic\\_club\\_ofcanada-may162017.html?undefined&wbdisable=true](https://www.canada.ca/en/health-canada/news/2017/05/economic_club_ofcanada-may162017.html?undefined&wbdisable=true)
- <sup>15</sup> Drummond MF, Sculpher MJ, Torrance G, et al. *Methods for the Economic Evaluation of Health Care Programmes*. (3rd ed.) New York: Oxford University Press, 2005: 1.
- <sup>16</sup> World Health Organization, Workbook 8, Economic Evaluations, 2000  
([http://apps.who.int/iris/bitstream/10665/66584/9/WHO\\_MSD\\_MSB\\_00.2i.pdf](http://apps.who.int/iris/bitstream/10665/66584/9/WHO_MSD_MSB_00.2i.pdf) accessed on May 30th 2017)
- <sup>17</sup> Husereau D, Drummond MF, et al., Consolidated Health Economic Evaluation Reporting Standards (CHEERS) – Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluation Publication Guidelines Good Reporting Practices Task Force, *Value in Health* 16(2013) 231-250
- <sup>18</sup> Source: Avinash K. Dixit & Robert S. Pindyck. *Investment Under Uncertainty*. Princeton University Press, 1994, 488 pp.
- <sup>19</sup> Gafni A. “The quality of QALYs (quality-adjusted-life-years): do QALYs measure what they at least intend to measure?” *Health Policy*. 1989 Oct;13(1):81-3. <https://www.ncbi.nlm.nih.gov/pubmed/10296157?dopt=Abstract>
- <sup>20</sup> Knapp M. “Economic outcomes and levers: impacts for individuals and society” *Int Psychogeriatr*. 2007 Jun;19(3):483-95, <https://www.ncbi.nlm.nih.gov/pubmed/17391570>.
- <sup>21</sup> Quality-adjusted life-years lack quality in pediatric care: a critical review of published cost-utility studies in child health. *Pediatrics* 115(5):e600-614.
- <sup>22</sup> Drummond M, Barbieri M, Cook J, Glick HA, Lis J, Malik F, Reed SD, Rutten F, Sculpher M, Severens J: Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report. *Value Health*. 2009, 12 (4): 409-418.
- <sup>23</sup> The Canada Opportunity, The Economy and the Growth Agenda; Government of Canada. November 2016  
[http://www.international.gc.ca/investors-investisseurs/assets/pdfs/download/The\\_Canadian\\_Opportunity.pdf](http://www.international.gc.ca/investors-investisseurs/assets/pdfs/download/The_Canadian_Opportunity.pdf)
- <sup>24</sup> Minister Philpott in her speech of May 16th at the Economic Club of Canada: [https://www.canada.ca/en/health-canada/news/2017/05/economic\\_club\\_ofcanada-may162017.html?undefined&wbdisable=true](https://www.canada.ca/en/health-canada/news/2017/05/economic_club_ofcanada-may162017.html?undefined&wbdisable=true)