July 30, 2020

Mr. Douglas Clark
Executive Director
Patented Medicine Prices Review Board
1400 - 333 Laurier Avenue West
Ottawa, ON K1P 1C1

RE: Roche Canada Input on PMPRB June 2020 Draft Guidelines Consultation

Dear Mr. Clark:

On behalf of Hoffmann-La Roche Limited ("Roche Canada"), please find enclosed feedback to the Patented Medicines Prices Review Board ("PMPRB") as part of the PMPRB Guidelines Consultation process.[1]

As a preliminary matter, as a member of both Innovative Medicines Canada ("IMC") and BIOTECanada, Roche Canada has reviewed the submissions from our industry associations and adopts and endorses them. In particular, Roche Canada agrees that Justice Manson's June 29, 2020 decision in *Innovative Medicines Canada v. Canada (Attorney General)*, 2020 FC 725, requires the PMPRB to fundamentally rethink its proposed Guidelines approach. This decision makes it clear that the PMPRB may not access third-party payments, or "rebates". The "maximum rebated price" (MRP) concept is central to the Guidelines and is inextricably linked to the new economic factors, and since that the MRP depends on (improper) access to third-party payments, a wholesale reconsideration of the proposed Guidelines is required in order to comply with Justice Manson's ruling.

Roche Canada therefore agrees that, given recent developments, the PMPRB must temporarily suspend the current consultation and re-release a Guidelines package that is consistent with regulatory tools that are within its mandate.

If implemented without major changes, one of Roche Canada's key concerns with the current draft PMPRB guidelines is the ability to bring innovative medicines to Canada. Canada competes with the rest of the world in attracting clinical research investment. Consistent with Roche's submission of the draft PMPRB guidelines in February 2020, the pricing reforms continue to send a message to global decision-makers that innovation and the advancement of patient-care is not a priority for Canada, thereby putting at risk our ability to compete for clinical research investments on the global stage and potentially limiting Canadian patients' early access to improvements in care.

[1] Roche Canada is committed to constructive engagement with the PMPRB on the draft Guidelines, however our response to this consultation is not intended and should not be interpreted as supporting the amendments to the Regulations or current Guidelines proposals. On June 29, 2020, the Federal Court of Canada declared that subsection 3(4) of the amended Regulations on the net price calculation is invalid, void, and of no force and effect for being *ultra vires* the Patent Act. Roche Canada continues to have grave concerns about the practicality and legality of the remaining amended Regulations. Roche Canada reserves the right to oppose any aspect of the amended Regulations or Guidelines that exceed the jurisdiction of the Board.

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Two recent publications further outline the unintended consequences of the new PMPRB guidelines. The first publication, authored by the Canadian Health Policy (Yanick Labrie, June 2020)[2] shows a significant negative relationship between price controls and pharmaceutical R&D investment or access to innovative drugs. This systematic literature review not only reveals fewer numbers of drug introductions as a result of pricing controls but also potential delay in drug launches by as much as 80%. The second publication, authored by the Office of Health Economics (OHE), identified critical limitations in using pharmacoeconomics to regulate the prices of new medicines (Berdud and Towse, July 2020)[3], as utilized by the PMPRB in the guidelines. In this paper, the OHE outlines a new approach to the threshold / PVT and warns that adoption of a supply-side threshold for pricing purposes could lead to a reduction in societal benefit, a reduction in research and development, inefficient resource allocation, and reductions to patient access. The research demonstrates the need to optimize the threshold with the incorporation of the sunk costs of research and development, the bargaining power of the payer, the competitive market dynamics, and the dynamic nature of healthcare budgets. Pharmaceutical pricing regulation should be informed by an understanding of the economic market structure that brings healthcare innovations to patients.

The prices of products negotiated with pCPA reflect the value they deliver to patients, their families and society. When setting prices and discounts for individual medicines, manufacturers consider a number of factors including the clinical benefit relative to available alternatives, the level of medical need addressed, the competitive situation in the market and the ability of the healthcare system to afford new medicines. The prices manufacturers set allow them to continue to invest in research and development of innovative diagnostics and medicines that can transform patients' lives, while supporting the financial sustainability of healthcare systems. Through negotiations, different value based approaches (outside of simple net discounts) are explored in order to reach a feasible option for both the manufacturer and participating provinces. These types of agreements are important and they serve value to patients and health systems. If the proposed guidelines require a net discount greater than the limits set out by the global organization, it would halt those discussions in Canada and would limit the number of choices that patients have. These proposed changes would have negative upstream and downstream effects resulting in fewer Canadian clinical trials and many job losses in Canada's life sciences sector. If there are no prospects for reasonable reimbursement, then it would be unethical to put patients on clinical trials knowing that they would come off the drug in the future given there is no reimbursement in Canada. Furthermore, heightened business uncertainty and aggressive cost-containment measures will significantly delay, if not prevent, the launch of any innovative drugs already set to enter the Canadian market.

Existing Challenges From Previous Draft Guidelines

There is an overarching concern as PMPRB staff are not bound by the guidelines and therefore reduced certainty for patentees regarding how these guidelines will be operationalized. Expanding upon IMC's comments on the significant information gap, Roche would also like to highlight outstanding issues from the previous draft guidelines.

Significant Concerns with CADTH Reanalyzed ICERs to set the MRP:

As outlined in the proposed guidelines, PMPRB will rely on CADTH's reanalyzed ICERs to set the MRP for "high cost", Category 1 medicines. Roche has significant concerns with this approach. First, there is a lack of clarity on which ICER would be used to set MRP when there are multiple

[2] https://www.canadianhealthpolicy.com/products/evidence-that-regulating-pharmaceutical-prices-negatively-affects-r-d-and-access-to-new-medicines-.htm
[3] https://www.ohe.org/publications/bargaining-approach-theory-icer-pricing-and-optimal-level-cost-effectiveness-threshold

ICERs reported by CADTH. For a given product, ICERs can vary significantly based on relevant scenarios, comparators and other modelling assumptions and result in a significant impact to the MRP as illustrated in Roche's February 2020 submission in response to the previous draft PMPRB guidelines. Pharmacoeconomic models that are used to derive ICERs are highly subjective and are driven by the model inputs and assumptions and thus significant differences are observed in manufacturer base case and CADTH reanalyses; for example CDR-reanalyzed ICERs were 780% higher on average compared to manufacturer submitted ICERs (see Appendix 1). This results in a lack of predictability for the MRP, before a product is launched into the Canadian market. This unpredictability will lead to delays in launch timelines, and in the worst case, may result in a decision not to launch in the Canadian market.

In the case where an HTA submission is not made, the draft guidelines stipulate that an automatic 50% discount be applied to the MLP. It is unclear why a decision not to seek public funding should lead to reductions in the price by 50%. There are many reasons why a manufacturer would not pursue a CADTH submission immediately, or to submit at all, and can depend on global/local resource availability, global allocation of resources to the Canadian affiliate, and/or chance of regulatory approval. As regulatory approval does not guarantee a positive CADTH recommendation or funding, manufacturers will need to seriously consider the risks of seeking regulatory approval for subsequent indications in the Canadian market. As simply seeking Health Canada approval may negatively impact price, it is expected that there will be a delay in patient access and/or a decision to not launch in the Canadian market at all.

Lack of Clarity Around Relevant Indication

As mentioned in Roche's February 2020 submission and meeting with the PMPRB, disease prevalence is an important determinant of product categorization and relevant indication; however, there is often limited Canadian specific data on disease prevalence. For many diseases, especially rare diseases, there is also variability in epidemiological estimates of prevalence based on the methods used in the study and variability depending on the testing used to identify disease subtypes. Regardless of the methods used to estimate prevalence, from the guidelines, it is unclear how specific patient population prevalence will be determined. For example, would prevalence be assessed based on the number of patients with a particular type of cancer? Or would it be limited to those patients with a specific biomarker? Or would it be limited to the number of patients eligible for the treatment based on the approved indication (including line of therapy)? Additionally, for many cancers, there are estimates for one-year, five-year and ten-year prevalence which would lead to different results for categorization and relevant indication.

Although PMPRB has considered the ability to increase price based on relevant indication, the implementation of such a price increase is not feasible given the current contractual obligations with payers where there is no process to go back to the provinces to request a higher price.

<u>New Challenges in Current Draft Guidelines</u>

The June 2020 draft PMPRB guidelines also introduce a number of new challenges which need to be considered and are not limited to the topics Roche has highlighted below.

The Use of Non Excessive Average Price (NEAP) for Grandfathered Products

The June 2020 draft guidelines proposed that the Maximum List Price (MLP) for grandfathered products be set based on the lower of Non Excessive Average Price (NEAP) and Highest International Price (HIP). NEAP does not accurately represent the average transaction price as it includes other types of transactions such as free goods and credits. Price tests relating to grandfathered products should be consistent with the approach taken before the implementation of

new guidelines. To retroactively apply these changes does not allow the manufacturer to also go back and revisit the decisions that were made based on the prior rules. Therefore, the NEAP should be removed from the draft guidelines, and the HIP for the PMPRB11 countries should be used to set the MLP for all grandfathered products.

Therapeutic Criteria Level (TCL)

Roche has significant concerns about the introduction of therapeutic class levels when setting MRP for New Patented Medicines. Historically, the vast majority (95%) of new medicines have been categorized as either 'slight/no improvement' or 'moderate improvement' by the PMPRB. With the additional criteria being proposed to define each therapeutic category, even fewer drugs would fall into 'breakthrough' or 'substantial improvement' thus pushing new medicines into lower therapeutic tiers and correspondingly lower MRP floors. Moreover, once a product is launched and the HTA recommendations and reports are released, competitors would be able to estimate the TCL levels and Pharmacoeconomic Price (PEP) values in order to determine the floor MRP. This poses a significant risk to pricing confidentiality (See Appendix 2).

Transparency of Maximum Rebated Price (MRP)

The transparency and ability to easily derive the MRP using public information is a concern for manufacturers. As noted above, based on the historical categorization of new medicines by the PMPRB, most products are expected to fall under Therapeutic Criteria Level 4. This provides a benchmark and increases the ability to estimate the TCL in addition to the publicly-available CADTH recommendations and economic reports with PEP calculations - ultimately allowing competitors to determine MRP of a new launch product. There would also be full transparency of MRP floor for files with no CADTH submission as per section 62 of the guidelines. In addition, for Category 1 products with market size over $50M, the MRP would be transparent as median dTCC would most likely fall below the proposed floors. It is important to note that the "floor" that is proposed is misleading since market size adjustments result in discounts that are lower than the proposed TCL floor which again, can be easily calculated using sales data.

Roche would like to further question the appropriateness of using median dTCC to set the MRP of high cost products that have specifically submitted a cost minimization model for their pharmacoeconomic analysis. By definition, cost-minimization analyses are only applied when interventions being compared are considered equivalent in terms of all relevant outcomes. The application of this test in this setting would therefore penalize new entrants into a therapeutic area and reduce options for patients.

Timelines / Implementation Challenges

The previous sections highlighted significant challenges with regards to the content of the revised guidelines. Assuming those parts of the guidelines are adopted, there are also numerous hurdles when it comes to implementing and operationalizing these changes. A particularly challenging aspect are the timelines, whether it applies to reporting and compliance or MRP assessment.

The revised draft guidelines are not clear on the specific time point the various prices would be determined, and when there is clarity, some are simply infeasible for manufacturers. For example, notwithstanding that Roche strongly disagrees that a 50% discount should be applied to the MLP based on not submitting to CADTH, the guidelines are not clear at which point PMPRB will determine the MRP of a patented medicine.

The draft guidelines attempt to set MRP for both the public and private markets, without truly understanding how the nuances of the private market - the number of insurers and thousands of different plans, their capabilities to implement PLAs, the timelines in which they can implement PLAs, as well as the ability to track utilization and process invoices. Lastly, all jurisdictions operate in a different manner, and process rebates at different timelines, making it impossible for manufacturers to achieve compliance in some cases. Appendix 3 showcases some examples highlighted above, and provides more details.

Major issues that were raised in the previous draft guidelines still remain and the updated draft guidelines have introduced more complexity. Our key concern continues to be our ability to launch innovative products, continue to conduct clinical trials, and advance medical science in Canada. The lack of clarity on several factors and the absence of the amended *Patentee Guide to Reporting/Online tool* makes it challenging for manufacturers to access the full impact of new guidelines.

In light of recent events, Roche Canada proposes that the PMPRB temporarily suspend the current consultation, form technical working groups to address the challenges before implementation. and re-release a Guidelines package that is consistent with regulatory tools that are within its mandate.

Regards,

David Shum
Director, Market Access and Pricing
Roche Canada

APPENDICES

Appendix 1: Issues with PEP/CADTH analyses

Key Issues

- Since the last consultation, there still remain a list of outstanding questions regarding the use of pharmacoeconomic factors in setting MRP
- Almost half of recent CADTH recommendations include multiple ICERs (Incremental Cost Effectiveness Ratios) leading to variability in PEP calculations
- Economic models are highly subjective and are sensitive to model inputs and assumptions leading to reduced predictability of MRP when launching new medicines
- CADTH reanalyzed ICERs are significantly higher than the pharmacoeconomic thresholds set by PMPRB thus MRP will be set by the floor rather than the PEP

Multiple ICERs reported by CADTH

As outlined in the Roche Response to the November 2019 proposed guidelines, depending on what is considered the most relevant comparator, the value for PEP (and subsequently the MRP) will be different. This leads to a lack of predictability in estimating the PEP (See Case Study 3 from previous consultation response[4]).

In an analysis assessing CADTH recommendations issued between Jan 2017 to December 2019, **49% of the files included more than one ICER**. These multiple ICERs would stem from different populations, different comparators and other scenarios. This raises the issue of which ICER would be used when assessing PEP and introduces significant unpredictability to manufacturers.

Subjectivity of Economic Models

"All models are wrong; some are useful" - George E.P. Box

Economic models are inherently subjective and their results are directly related to model inputs and assumptions. There is an observed difference between manufacturer submitted ICERs and CADTH reanalyzed ICERs. Looking at CADTH recommendations from Jan 2017 to Dec 2019, pCODR re-analyzed ICERs were **75% higher** than manufacturer submitted ICERs. CDR-analyzed ICERs were **780% higher** on average compared to manufacturer submitted ICERs (Roche, Data on file).

The predictability of PEP of a new drug into the Canadian market becomes very difficult when CADTH reanalysis is hard to predict. Given the subjectivity of economic models, it raises the question whether economic models should be used as a price setting tool at all.

CADTH Reanalyzed ICERs

Looking at CADTH recommendations from Jan 2017 to Dec 2019[5], the average CDR reanalyzed ICER (numeric) was $1,292,998/QALY and $291,262/QALY for pCODR. These averages are much higher than the PVTs set by PMPRB. The proportion of ICERs above the $150,000/QALY threshold was 61% for CDR and 64% for pCODR. The proportion of ICERs above the

[4] https://www.canada.ca/content/dam/pmprb-cepmb/documents/consultations/draft-guidelines/submission received/2020_02_Guideline%20Consultation%20Submission_Hoffman-La%20Roche%20Ltd.pdf

[5] Roche, Data on file

$200,000/QALY threshold was 48% for CDR and 52% for pCODR. Thus, it is reasonable to assume that when setting MRP, many drugs will be pushed down to the level of the floor reduction as they would have CADTH reanalyzed ICERs that are much higher than the PVTs set by PMPRB.

	CDR	**pCODR**
Total numerical ICERs	79	44
Average numerical ICER	$1,292,998/QALY	$291,262/QALY
Proportion of ICERs > $150,000/QALY	48 (48/79 = 61%)	28 (28/44 = 64%)
Proportion of ICERs > $200,000/QALY	38 (38/79 = 48%)	23 (23/44 = 52%)

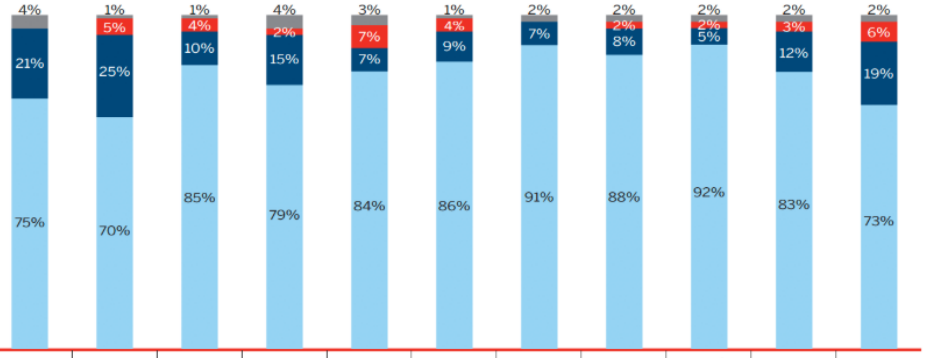
Appendix 2: Therapeutic Class Levels

- Historically, almost all (95%) of new patented medicines have been categorized as 'Slight/No Improvement' or 'Moderate Improvement'
- The additional criteria proposed in the classification of TCLs are subjective and restrictive and would allow for even less launch products being categorized as 'breakthrough' or 'substantial improvement'
- The TCLs can be estimated by competitors with high confidence based on the definitions of the classification and publicly available information

Historical Trends

In order to understand the historical trends associated with new patented medicines and their associated therapeutic benefits as viewed by PMPRB, we looked at the most recent annual report from PMPRB. From 2010-2018, the majority of new medicines were classified as 'Slight/No Improvement' at 83%. Out of new medicines, 12% were classified as 'Moderate Improvement'. 'Substantial Improvement' and 'Breakthrough' classifications were given to 3% and 2% of new medicines respectively. Thus, 95% of new medicines were classified as 'Slight/ No Improvement' or 'Moderate Improvement'.

Figure 1. Breakdown of New Patented Medicines by Therapeutic Benefit



NUMBER OF NEW PATENTED MEDICINES BY THERAPEUTIC BENEFIT	2010 INTRO	2011 INTRO	2012 INTRO	2013 INTRO	2014 INTRO	2015 INTRO	2016 INTRO	2017 INTRO	2018 INTRO*	OVERALL 2010–2018	OVERALL 2010–2018 REVENUE SHARE
Slight/No Improvement	51	76	70	91	87	73	116	52	56	672	73.1
Moderate improvement	14	27	8	17	7	8	9	5	3	98	19.3
Substantial Improvement	0	5	3	2	7	3	0	1	1	22	5.7
Breakthrough	3	1	1	5	3	1	3	1	1	19	1.0

* Assessment as of March 31, 2019

Source: https://www.canada.ca/en/patented-medicine-prices-review/services/reports-studies/annual-report-2018.html

Additional Criteria Proposed for Therapeutic Class Level Classification

The June 2019 guidelines include additional factors to be considered when assessing the therapeutic class levels for new medicines. The highlighted text in the table below refers to the new criteria proposed. These new criteria are currently not listed as primary or secondary factors in the PMPRB Compendium of Policies, Guidelines and Procedures.

Therapeutic Level	Current Definition	Proposed Definitions in June 2020 Guidelines
I	**Breakthrough:** A breakthrough drug product is the *first one* to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication.	The patented medicine is the *first medicine* to be sold in Canada that effectively treats a particular illness or effectively addresses a particular indication in a clinically impactful manner. Clinically impactful improvement includes improvements in quality of life, mortality or significant reductions in disease severity or healthcare utilization, preferably based on high quality evidence using hard clinical endpoints rather than surrogate outcomes. A high QALY gain is normally associated with medicines at this level.
II	**Substantial Improvement:** A drug product offering substantial improvement is one that, relative to other drug products sold in Canada, provides *substantial improvement* in therapeutic effects.	The patented medicine provides a *considerable improvement* in therapeutic effect, relative to other medicines sold in Canada, in a clinically impactful manner. Clinically impactful improvement includes improvements in quality of life, mortality or significant reductions in disease severity or healthcare utilization, preferably based on high quality, active-comparator controlled evidence using hard clinical endpoints rather than surrogate outcomes. High quality network-meta-analysis may also be considered. A high QALY gain is normally associated with medicines at this level.
III	**Moderate Improvement:**A drug product offering *moderate improvement* is one that, relative to other drug products sold in Canada, provides moderate improvement in therapeutic effects.	The patented medicine provides *moderate absolute improvement* in therapeutic effect, relative to other medicines sold in Canada. The medicine may have (a) an increase in clinically relevant efficacy; (b) be associated with a reduction in the incidence or grade of important adverse reactions; or (c) be associated with clinically relevant increased ease of use characteristics (e.g. route of administration, convenience, increased compliance, etc.), however, these improvements may provide limited meaningful clinical impact or may be based on lower quality clinical evidence. Patented medicines at this level are normally associated with moderate incremental QALY gains with a relatively high degree of certainty or a high QALY gains with a relatively low degree of certainty.
IV	**Slight or No Improvement:** A drug product offering *slight or no improvement* is one that, relative to other drug products sold in Canada, provides slight or no improvement in therapeutic effects.	The patented medicine provides *no or slight improvement* relative to other medicines sold in Canada. Alternatively, or in addition, the patented medicine has very limited (or no) robust clinical evidence available to clearly identify a medicine's degree of clinically relevant therapeutic improvement relative to other medicines sold in Canada. Limited or no additional QALY gains or significant uncertainty due to poor quality evidence are associated with medicines at this level.

Clinical Endpoints

Medicines that are the first to treat a condition would not necessarily have hard clinical endpoints. In fact, some orphan drugs would fall into this category of being the first drug to treat a certain disease and research has shown that trials for orphan drugs use surrogate outcomes and they tend to be non-randomized and unblinded[6]. For some products, hard clinical endpoints are not feasible, and surrogate markers for those endpoints have been widely accepted by regulatory bodies and practitioners.

QALY gains

The use of QALYs in economic evaluations has been under debate for years. Some argue that QALYs don't capture all the relevant health benefits of a treatment such as convenience, non-health related benefits and effect on caregivers and thus underestimates the full range of benefits associated with a new technology[7]. There are also arguments that 'a QALY is a QALY is a QALY' is not true and valuations attached to loss in quality of life may differ by age[8].

'High QALY gain' is a subjective term and the QALYs gained is a function of the economic model inputs, time horizon and other assumptions. By varying the model inputs, the number of QALYs gained can easily be altered. Thus, QALY gain, if captured from an economic model, would not be an objective measure and thus should not be used for TCL classification. To illustrate this point, let's look at two drugs that were recently categorized as 'Breakthrough':

Example 1: Sebelipase Alfa (Kanuma) for lysosomal acid lipase (LAL) deficiency

	Population	**Delta Cost ($)**	**Delta Outcomes (QALY)**	**ICER**
CADTH Reanalysis	Infantile	$177,558,521	35.91	$4,944,000/QALY
	Pediatric/Adult	$40,104,683	17.84	$2,274,000/QALY

[6] Kesselheim, A.S., J.A. Myers, and J. Avorn, Characteristics of clinical trials to support approval of orphan vs nonorphan drugs for cancer. Jama, 2011. 305(22): p. 2320-6.

[7] Prosser, L.A., J.K. Hammitt, and R. Keren, Measuring health preferences for use in costutility and cost-benefit analyses of interventions in children: theoretical and methodological considerations. Pharmacoeconomics, 2007. 25(9): p. 713-26.

[8] Weinstein, M.C., A QALY is a QALY--or is it? J Health Econ, 1988. 7(3): p. 289-90.

Looking at the CADTH analysis, Sebelipase Alfa had ICERs of $4.9M/QALY and $2M/QALY for infantile and pediatric/adult populations, respectively. The incremental effects associated with those ICERs were 35.91 and 17.84. Would these be considered 'high QALY gains'? Even though the QALY gains may be numerically high, note that the ICERs themselves are far greater than the Pharmacoeconomic Value Thresholds (PVTs) set by PMPRB.

Example 2: Midostaurin (Rydapt) for Acute Myeloid Leukemia

	Delta C	**Delta E**	**ICER**
CADTH Reanalysis	$18,049	0.80	$22,579/QALY

Another product that has received 'breakthrough' TCL by PMPRB in Midostaurin, The CADTH reanalysis for Midostaurin resulted in an ICER of $22,579/QALY. The 'QALY gain' associated with this product was 0.8. Would this be considered 'high QALY' gain? Even though the incremental effect was measured to be 0.8, the ICER itself is favourable. Thus, QALY gains should be removed as a criteria for TCL determination. It is highly subjective and is driven by model inputs and using it in price setting scenarios would lead to nonsensical conclusions.

Network Meta Analysis

Under the definition of 'substantial improvement', there is a mention that a "high quality network meta analysis" may also be considered. In general, the results of NMAs have a high degree of uncertainty and caveats associated with them. Thus, they should be used with extreme caution especially in scenarios where they are being used to determine the floor of a net price.

Predictability of TCL

Given the proposed definitions of TCLs, it would be fairly easy for a competitor to determine the level that a given product would fall under. Once a product is launched and especially once HTA recommendations and detailed reports are posted publicly, more information about new proposed criteria can easily be extracted from these sources. Thus, when combined with the CADTH reports and the best estimate of TCL level, a competitor can easily estimate the floor net price which poses a huge threat to confidentiality.

Appendix 3: Timelines and implementation Challenges

Impact of Proposed 2020 Guidelines

- Timelines of reporting and compliance and MRP assessment cannot be incorporated into the existing CADTH / INESSS / pCPA processes in a feasible manner based on the June 2020 draft guidelines

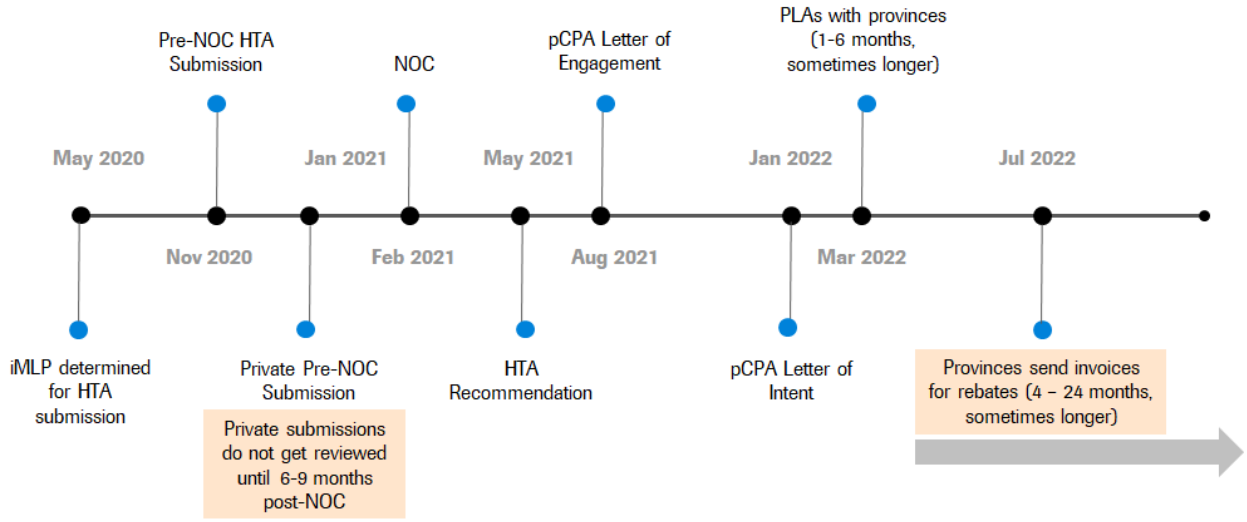
Example 1: No HTA Submission at NOC

While most manufacturers will choose to submit a dossier to HTA pre-NOC or at NOC, there are cases where a submission is not made until much later. The HTA submission can be made at any time, whether it's a few months after NOC, or years after NOC.

The guidelines are not clear at which point PMPRB will determine the MRP of a patented medicine, and how long of a window the manufacturer has before an automatic 50% discount is applied to the MLP.

Example 2: Overall MRP Timeline

The overall timeline for how MRP is implemented is by far the most problematic, and does not fit in with existing frameworks and processes that are in place. Below is a graph of a typical timeline for a manufacturer, taking into consideration Health Canada, CADTH / INESSS, pCPA and provincial listings.



The guidelines fail to consider many elements of the existing process, making the implementation of MRP to be not only confusing, but infeasible.

1. **Private Market** - private submissions are usually filed ±3 months of regulatory approval, with an average review time of 6-9 months. At the end of the review period, a decision is made on whether or not the private plan will cover the drug. If a PLA is required, this process can take up to another year due to the number of private companies and the lack of capacity and/or ability to implement PLAs.

2. **MRP** - Based on the draft guidelines, MRP / MRP[A] would be re-assessed annually. The MRP can either be determined based on PEP, or based on the median dTCC, depending on the case. However, for MRP that is dependent on PEP, it is not possible to re-assess MRP annually unless there is an updated CUA available. While MRP[A] can be adjusted annually based on actual sales, MRP should always remain consistent where PEP is involved.

3. **pCPA and PLAs** - pCPA negotiations typically begin a few months after a final HTA recommendation has been published and length of negotiations can vary. Following the completion of negotiations, some jurisdictions are quick to finalize pricing contracts in order to fund a product, while others lack the resource to do this in a timely manner. The process in implementing PLAs can take anywhere from a month to years. Additionally, while some invoices will be sent to manufacturers a couple of months after the quarter ends, others could take up to 2 years, particularly if an invoice is based on annual terms. This poses a significant issue in terms of reporting and compliance.

Summary:

There are many factors to consider when it comes to implementing a high-impact factor such as the MRP. As PMPRB is proposing a set of guidelines that encompasses list price, net price, public market, private market and more, with pricing rules that are dependent on the timing of other countries' launches and when Canadian jurisdictions can implement PLAs and process rebates, it is critical that more thought be given to incorporating MRP into the existing process and framework in a feasible manner for all parties involved.