Patented Medicine Prices Review Board (PMPRB) Guidelines Modernization: Discussion Paper – HepCBC Comments - October 30, 2016

HepCBC Hepatitis C Education and Prevention Society is a registered non-profit patient group which has been around since the late 1990s. We are made up mostly of volunteers with lived experience of hepatitis C, operating without any funding from provincial or federal governments. Our mission is to provide education, prevention, and support to those living with hepatitis C. Our goal is to eliminate hepatitis C from the face of the earth, starting in British Columbia.

(1) What does the word "excessive" mean to you when you think about drug pricing in Canada today? For example:

(a) Should a drug that costs more annually than a certain agreed upon economic metric be considered potentially excessively priced?

ANSWER: Yes – economic metrics are of great value in flagging possible excessive pricing. For example, if the annual cost of a new drug is double the cost of another in the same class (both sold in Canada), PMPRB would definitely have to investigate. However, this investigation could uncover reasonable justification for the increase.

Conversely, we cannot depend totally on current economic filters to flag excessive pricing. There could be cases in which drugs which are excessively priced may not be "caught" by PMPRB's current economic metrics. Such drugs could actually be priced much lower than they are now because those who set the ceiling price did not accurately take into account the prevalence of the disease, or a radical increase in demand due to increased efficacy, factors which would greatly affect the number of treatment packages sold. In these cases, there is no reason to allow "orphan drug" pricing for conditions which have a large potential treatment population.

For example, with hepatitis C very few people took the older treatments with extremely harsh side effects and low efficacy; doctors advised most patients to wait for new, improved drugs (the 'warehousing' phenomenon). Once the new drugs became available, demand for them skyrocketed. This might have been predicted by PMPRB if prevalence was factored in as an economic metric. Note that this is complicated by the lack of accurate, up-to-date surveillance data showing how many people have chronic hepatitis C in Canada. In order to factor in prevalence as part of an economic metric, PMPRB would require up-to-date and accurate epi-/prevalence data for the disease in question, something which Canada may need to prioritize (and budget for) in a federal strategy for lowering our country's pharmaceutical costs.

(b) Should a drug which costs exponentially more than other drugs that treat the same disease be considered potentially excessive?

ANSWER: Perhaps. This depends on comparable therapeutic value, comparable side effects, balanced by whether there is now a greater number of patients who are now eligible for, or requesting, treatment – in consideration of a potential "economies of scale" benefit to pharma.

Also, there is the issue of the time required for treatment. For example, even though new hepatitis C drugs may cost $750 per pill, the number of pills required per day is down from several to one, and the treatment time is vastly reduced (from 48 weeks

down to 8-12 weeks), which has made the cost of the old and new treatments comparable.

Finally, there is the issue of how to determine if pills treat "the same disease." For example, with hepatitis C quite different drug regimens are currently used according to the genotype, the degree of liver damage, co-infections and co-morbidities, etc.

(c) In considering the above two questions, does it matter to you if a very costly drug only treats a small group of patients such that it accounts for a very small proportion of overall spending on drugs in Canada?

ANSWER: Yes, for "orphan" drugs treating low-prevalence diseases (particularly if these diseases have serious impact upon – or threaten the lives of – patients) very high prices may be justified for at least long enough for developers to recoup their R&D costs. After that time, proportionately lower pricing should be considered. It is possible that a down-scaling model could be attached to initial pricing, slowly and incrementally lowering the price as the R&D costs are reimbursed.

(d) Conversely, if a drug's price is below an agreed-upon metric and in line with other drugs that treat the same disease, should it be considered potentially excessive if it accounts for a disproportionate amount of overall spending on drugs in Canada?

ANSWER: Yes; it is possible that the other drugs that treat the same disease are also excessively priced. Perhaps the agreed-upon metric is insufficient. Perhaps there are other factors such as greatly increased efficacy, fewer (or less serious) adverse events, or a broader (i.e., a national age cohort-based) screening campaign which could make some or all of these drugs more in demand by patients and their physicians, thus contributing to a far greater potential market than before current improvements were made. Again, improved economies of scale – due to high prevalence combined with an increased demand – would justify a reconsideration of pricing for the entire class of drugs.

(e) What economic considerations should inform a determination of whether a drug is potentially excessively priced?

SHORT ANSWER: A medication's price is "excessive" if it is not accessible to the people who need it.

DETAILED ANSWER: Looking at this question from a more systemic perspective, we would say that regardless of what the medication treats (i.e., a rare or common disease) and its price related to other medications of similar or different categories, medication price is considered to be "excessive" if provincial, territorial, and/or private payers have difficulty providing the medication to those who are medically considered to benefit from it (i.e., evidence-based treatment). More precisely, if, due to high cost of a medication plus high prevalence of the disease, the insurance plan needs to ration the medication in order to remain solvent (to avoid the choice of either bankruptcy or increasing premiums for all), then the medication price is considered to be excessive. For example, consensus guidelines for hepatitis C say that everyone with the condition should be considered for treatment. However, the cost is so high and the number of people requiring the medication so great that insurance payers in Canada generally impose a non-evidence-based requirement that patients prove liver damage of fibrosis level 2 (out of 4) or greater before payers will cover treatment. Conversely, if the prevalence is very low (as in an "orphan" disease) in order to allow pharma to recover its R&D costs, insurers can justify paying the high premium due to the small number of claims. The PMPRB must include factors such as

the prevalence of the illness, potential effects of broader screening for it, and potential benefits to population-health when considering the cost-effectiveness and the potential price of a drug.

We deal with the question of modelling these factors further in Question #10.

(2) Given that it is standard industry practice worldwide to insist that public prices not reflect discounts and rebates, should the PMPRB generally place less weight on international public list prices when determining the non-excessive price ceiling for a drug?

ANSWER: Yes, we would like to see less weight put on international pricing and more put on other factors such as prevalence. However, we recommend that PMPRB should continue to consider international public list prices in its benchmarking, as this contextual comparison is an important check and balance which benefits (or protects) both patients and pharmaceutical companies. However, we don't see it as the only criteria. See our further recommendations in our answer to Question 4.

(3) In your view, given today's pharmaceutical operating environment, is there a particular s.85 (Section 85 of the Patent Act) factor that the Guidelines should prioritize or weigh more heavily in examining whether a drug is potentially excessively priced?

ANSWER: In Section 85, we found many of the factors that we have discussed herein, with which we have no problems.

However, we were surprised that ***prevalence*** was not listed. We suggest that it be prioritized as #1 among all factors that are implicitly contained in Subsection (2) (b): "such other factors as may be specified in any regulations made for the purposes of this subsection or as are, in the opinion of the Board, relevant in the circumstances."

Also, we were surprised to find in Section 85 (3) the following subsection:

- **"Research costs**

  (3) In determining under section 83 whether a medicine is being, or has been, sold in any market in Canada at an excessive price, the Board shall not take into consideration research costs other than the Canadian portion of the world costs related to the research that led to the invention pertaining to that medicine or to the development and commercialization of that invention, calculated in proportion to the ratio of sales by the patentee in Canada of that medicine to total world sales. 1993, c. 2, s. 7."

The subsection above may – or may not – serve Canada, the pharmaceutical company, or patients well. We are not sure, but if there is a way to weigh it less heavily than others that might be beneficial. We simply call attention to this, as we do not have the expertise to determine its actual implications to pricing. We hope those who are more privy to the implications than we are will re-visit this subsection with critical yet open minds.

We support ***strict enforcement of any law setting a minimum % amount of pharma R&D that a company is to spend in Canada***. We prefer that pharmaceutical

companies be offered tax incentives for doing this rather than strict rules telling them what they must do, which are neither accurately monitored nor strictly enforced.

We also acknowledge that R&D costs may be lower in other countries, so requiring countries to do R&D in Canada may contribute to more costly drugs here, something patients do not generally like. At the same time, we do advocate for clinical trials to be held here in Canada. Clinical trials held in other countries may not be representative of the Canadian landscape in terms of the diversity of genotypes, transmission routes, or other factors. (more on this topic in Question #5)

(4) Should the PMPRB set its excessive price ceilings at the low, medium or high end of the PMPRB7 countries (i.e., the US, the UK, Sweden, Switzerland, Germany, France and Italy)?

ANSWER: We recommend that the PMPRB remove the USA from the PMPRB "7" as its high pricing generally skews the price radically higher. Canada should set its excessive price ceilings at the low end of this new PMPRB "6" in recognition that actual prices paid generally are significantly lower than those reported, due to lack of transparency regarding opaquely-negotiated discounts.

(5) Does the amount of research and development that the pharmaceutical industry conducts in Canada relative to these other countries impact your answer to the above question and if so, why?

ANSWER: No, it should not. Our reasons are twofold:
First, tying Canadian pharma R&D to pharma pricing has already been tried in Canada (in 1987 legislation which still stands), and from everything we have seen, it has failed all around. The 'carrot' of relinquishing compulsory licensing in return for companies locating in Canada and doing R&D in Canada was simply not attractive enough to pharma. And any 'sticks' – such as instituting PMPRB price ceilings – are simply not being used. We have ended up without the kind of R&D spending in Canada that pharma does in other countries such as USA and France. At the same time our prices are still disproportionately higher, even than prices in Europe, ***and we have given up (what had been) our sovereign right to invoke compulsory licensing (forcing pharma, before a patent has expired, to license generic version to be sold in Canada at much lower costs than patent drugs when deemed essential for Canadian public health).*** Companies are expected to spend 10% of annual revenues on R&D, but this is seldom the case, and seldom enforced (even according to a recent "Innovative Medicines Canada" webinar). Industry would probably like to see this expectation lowered or removed, and this is one area in which patient groups and industry would seem to be in agreement. However ***lowering or even removing entirely the "R&D in Canada" expectations should be tied to reinstating that compulsory licensing can be invoked by Canada in certain cases***.

Second, there are other R&D-related and similar considerations:

(a) Is the R&D actually being done in Canada, or in some other country? (This should be carefully monitored and publicly reported, presumably by PMPRB).

(b) How are the R&D dollars being spent in Canada – is the R&D being done

disproportionately in one therapeutic class over others? (Canada could occasionally establish priority R&D areas in which they give tax incentives for R&D done in Canada for a specific therapeutic class that they feel is under-represented, or for research that Canada wants to see but that pharma may regard as non-lucrative. Examples could be a hepatitis C vaccine for IVDU or users of dialysis, or a combined hepatitis B/C oral Point-of-Care test for immigrants from endemic countries.)

(c) Is Canada giving tax incentives to companies according to what they spend on Canadian patients (i.e., in the form of compassionate care or co-pay rebates to individuals), in grants to Canadian researchers (in universities or small startups) or in grants to Canadian disease-specific physician, nurse, or patient groups?

Our general recommendations would be that encouraging pharmaceutical R&D within Canada should be handled by Revenue Canada like any other incentivized investment, possibly in consultation with Health Canada or PMPRB. The current system would seem to be broken; and because it ties R&D in Canada to drug pricing (justifying not invoking compulsory licensing), it could be seen as contributing to our current high drug prices.

Certainly the individual drug's R&D costs should be considered in any pricing model, but not whether the pharma involved is putting "X" % of its annual revenues into Canada-specific (or any particular country's) R&D. To this pharma would rightfully say that there are many research 'dead ends' for every one blockbuster drug, and that this necessary but non-lucrative research should be considered in the pricing model. As a patient group, we understand and support that argument. So the amount listed as R&D costs in the pricing model could be "X" % higher than the actual R&D cost for the drug in question, "X" to be determined through consultation among stakeholders and revisited every 10 years or so as needed.

(6) What alternatives to the current approach of categorizing new patented medicines (based on degree of therapeutic benefit) could be used to apply the statutory factors from the outset and address questions of high relative prices, market dynamics and affordability?

ANSWER: We question the argument that a new medication, even if it's in a completely new class of medicines, with high success rates and few side effects, should be priced higher than previous medication(s) prescribed for the same condition. This metric leads to artificially-inflated drug prices. As technology improves over time, it is a given that new classes of medication which can cure a disease will be developed. An example is the genetic therapy that will be developed in the future, and will likely be an actual cure.

We contend that a variety of key stakeholders should be involved in determining a fair yet equitable profit margin, whether it be a % or an actual value, to ensure the price of a new medication does not get out of control. We deal with the question of a fair and equitable profit margin further in Question #10.

One key issue with setting a new price ceiling for a new medication is that the ceiling price of the comparator medication does not go down (or get adjusted post-market) even if a generic is available for the comparator. Hence, the ceiling price of the new medication is based on the originally-set ceiling price of the comparator medication, and *is not reflective of the actual selling price of the comparator medication.* Alternatively, the new ceiling price

of the new medication could be set based on the market price (or a specified maximum percentage thereof) of the previous Canadian *generic* version, rather than the ceiling price of the previous brand medication. If no generic version is available, an estimated average maximum generic price could be computed from the patent price (this is a % of the patent price – note that each province uses a different % formula so an average would have to be used at the federal level).

This brings us to the question of generic pricing, which PMPRB does not regulate, yet it is an area of great concern both to PMPRB and to this audience as per the following article in the STAR and one we feel must be at least mentioned in this review: https://www.thestar.com/opinion/commentary/2016/02/17/canada-is-needlessly-bleeding-money-on-generic-drugs.html.This refers to **PMPRB's "GENERICS 360"** report which we also commend highly: http://www.pmprb-cepmb.gc.ca/CMFiles/NPDUIS/NPDUIS_Generics_360_Report_E.pdf

(7) Should the PMPRB consider different levels of regulatory oversight for patented drugs based on indicators of risk of potential for excessive pricing?

ANSWER: Yes, this makes sense given the need to lower drug prices in order to preserve a high and equitable standard of care for all residents of Canada. However we cannot give a detailed answer to this question due to insufficient information about this process.

(8) Should the price ceiling of a patented drug be revised with the passage of time and, if so, how often, in what circumstances and how much?

ANSWER: Yes, this is a very critical point. The PMPRB should consider ways to drive down ceiling prices established at the introduction of a drug to market thereby establishing a more realistic price point at the onset. The PMPRB should be empowered with the ability to "re-bench" and re-evaluate the appropriateness of a medication's price (periodically, or under other circumstances such as the revision of indications surrounding a medication, a re-evaluation of the prevalence of an illness, or the establishment of improved disease management practices). As the price of a medication will likely go down over time, the ceiling price of a new medication should be based on the *actual* drop in price of the comparator medication (as we recommend, the average generic price of the previous version), *not* the pre-set ceiling price of the previous patent version (also see Question 6).

Other factors to consider over time:

(a) Changes in the Consumer Price Index

(b) Sustainability

(i) Is this drug for managing a chronic disease or is it a cure? If it is a cure, the drug will no longer be needed once everyone is cured so there is a greater need to recoup costs and make profits before the majority of patients are cured. Curing hepatitis C is a key example of this dynamic.

(ii) If curable, can patients be re-infected and if so what % of patients are at risk? This issue is, for example, a critical part of the care of patients with STIs.

(c) Competition (how much time is left on a patent, and are there other similar

competitor drugs now for sale?)

(d) Have R&D costs already been recovered? This is an interesting question because in order to prove that they have not yet recovered their costs, pharmaceutical companies may have to reveal their previously confidential pricing.

(e) International market (What is the prevalence of the disease in Lower, Middle, and Higher Income countries? Does the company which makes the drug sell to these markets and if so at what price?)

We greatly appreciate the data so carefully presented by the PMPRB in this recent poster specifically about hepatitis C drug pricing which shows the PMPRB is looking at some of these issues in great detail:
http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1249&lang=en

(9) Should price discrimination between provinces/territories (P/Ts) and payer types be considered a form of excessive pricing and, if so, under what circumstances?

ANSWER: Individual provinces price a medication differently depending on various factors, such as prevalence and the healthcare budget. This goes back to Question 1 where the price of a medication should be considered excessive if an individual province is unable to treat everyone who needs to be treated.

Moving between P/Ts can affect a patient's ability to pay for their medication, especially in cases where there are pronounced cost differences for a medication the patient uses regularly. As PMPRB's role is to set the price ceiling and it's up to individual P/Ts to implement healthcare (i.e., Canada is not a federal healthcare system), PMPRB's responsibility is not to consider an individual patient's ability to pay (i.e., that responsibility lies more with pCPA). However, this is an example where PMPRB, CADTH, pCPA, INESS, and the P/Ts need to develop and consider efficient methods to cover such cost differentials.

While we understand the rationale for confidential (opaque) price negotiations which result in different prices in the different P/Ts, the PMPRB must work with F/P/T and international parties to address and reduce disparities as a result of (confidential) negotiations at the level of the individual P/Ts.

(10) Are there other aspects of the Guidelines not mentioned in this paper that warrant reform in light of changes in the PMPRB's operating environment?

ANSWER: The model used for pharmaceutical pricing by PMPRB should include many more factors than simply therapeutic value and benchmarking with international prices. Several of these (such as ***prevalence*** and adverse events, broader screening, sustainability, competition, timing of patents and availability of generics, etc.) have been addressed through our answers herein. The costs of making, marketing, and distributing the medication must be built into the cost. And very importantly, the model should include an *"Ethical Profit Margin."* This means that pharmaceutical companies should be fairly compensated for their R&D, not only for the new medication, but for the many "dead ends" they had to follow in order to get there. They should also be compensated fairly enough that their shareholders are given a fair

to generous return on their investment. Government should give tax incentives to companies which re-invest in Canada. But pricing should be revisited every few years, and PMPRB should be free to make adjustments to the ceiling upon consideration of changing environment and conditions. ***The place of prevalence and related economies of scale in determining fair and ethical pricing cannot be overstated. Prevalence should include a consideration of the potential for use of the medicines in the international context as well as Canada.***

(11) Should the changes that are made to the Guidelines as a result of this consultation process apply to all patented drugs or just ones that are introduced subsequent to the changes?

ANSWER: As it is difficult implement a new policy for medications that were previously approved, changes that are made to the Guidelines should be applied primarily to the future ones. Any revision, patent-extension, or "evergreening" (the creation of incrementally small changes and improvements which result in a new or extended patent) of current medications will also be subject to this new policy. Since implementation of a new policy requires a period of time for all stakeholders to adjust, it is likely that currently-approved medications will have to undergo review (e.g., a revision) during/soon after that period of adjustment (e.g., 2-3 years).

(12) Should one or more of the issues identified in this paper also or alternatively be addressed through change at the level of regulation or legislation?

ANSWER: PMPRB, with its mandate to establish the ceiling price of a drug, does not technically duplicate the work of CADTH, CDEC, INESS, or pCPA. However, we question its relevance as a full stand-alone agency with such a limited role. CDEC currently assesses drug pricing as part of its recommendation to the P/Ts as to whether to list new medicines. Due to the potential overlap in research and analysis, there may be an improvement in efficiency if CDEC and PMPRB were eventually to merge. In this case, INESS would have to either accept the CDEC/PMPRB determination of ceiling price, or do its own independently.

Changes to guidelines, greater information-sharing and cooperation among the health agencies and possibly with Revenue Canada (regarding incentives), and streamlining of processes at the level of regulation are all essential in the short term to help regulate the price of Canada's medicines. However, only with legislative power can agencies be consolidated, their mandates changed, or sustainable and efficient drug pricing controls be set for the long term. For example, pCPA now oversees price negotiation for all biologics and biosimilars, and it is likely that more pricing control/negotiation for more medication categories will be included in the future. It is also quite possible that in the future, a federal agency will oversee the price negotiation for all medications across Canada. Hence, to make pCPA negotiations binding and to ensure all provinces can benefit from a lower price, legislative reform will be needed.

It is good that patient groups, as representatives of consumer-stakeholders, are being called upon to participate in this process. We contend that Canadian taxpayers, as funder-stakeholders, are highly invested in attaining fair pharmaceutical pricing in our country as it strongly affects their pocketbooks. Even though the way to arrange this is unclear, representation should be sought so that their missing voices can be included.