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Thank you for the opportunity to comment on the consultation on the proposed amendment to the Patented Medicines Regulations of the Patented Medicine Prices Review Board.

To begin with, although it is outside the mandate of this consultation and of the PMPRB itself, reforming the regulations is a poor second choice for controlling drug prices in Canada. The best way is a national pharmacare plan that would utilize monopsony buying power to achieve lower prices. Prices in both Australia and especially New Zealand are significantly lower than those in Canada and neither of these countries references their prices against those in other countries. The PMPRB should be reserved for situations where there is gross abuse of market power.

Specific comments on the proposed changes.

1. Introducing new factors to help determine whether a price is excessive

The statement that drugs that alone in their class will be in greater demand is based on the assumption that these drugs typically offer a significant therapeutic gain. This assumption is not necessarily correct.

A total of 426 drugs were approved by Health Canada between 1997 and 2012 and evaluations of their therapeutic value was available for 345 of these. Data on first in class status was available for 292 of these 345 drugs. Ninety-eight drugs were first in class and only 16 of these (16.3%, 95% CI 10.3, 24.9) were therapeutically innovative [1].

The discussion document from Health Canada says that in setting a price for new patented drugs there is a need to recognize the cost of R&D and manufacturing so that pharmaceutical companies are able to continue to invest in the production of new drugs.

First, there is considerable debate about how much it costs to bring a new drug to market. PhRMA, the organization representing the large multinational companies in the US, cites a figure of $2.6 billion, in 2013 dollars, to research and develop a new drug [2]. This figure comes from a study from the Tufts Center for the Study of Drug Development of 106 randomly selected new drugs obtained from a survey of 10 pharmaceutical firms [3]. However, this estimate is highly contested [4]. To begin with, the names of the drugs and all the development costs associated with them are confidential so that the authors' work cannot be independently verified. The drugs analyzed exclude any products that were co-developed with or licensed-in from another company. Almost half of the amount cited is opportunity costs, i.e., not money that was actually spent, but rather the "lost earnings" due to the fact that the money invested in R&D was not invested elsewhere (the opportunity cost of the investment). In a critique of an earlier estimate by the same authors, Light and Warburton raised a number of other issues about the methodology that was used including: the inherent comparability and reliability of the survey data due to variations in internal company cost allocation methods over time and across companies; the clear interest of pharmaceutical

companies in higher (rather than lower) estimates of drug development costs, and the sampled firms' likely awareness of the intended use of the survey data; the non-random sample of firms contributing research and development data; and the fact that the cost estimates were not adjusted for large public subsidies in the form of tax deductions and credits [5]. (DiMasi et al vigorously defended their calculations in a rebuttal [6].)
Second, as the table below shows, the price that companies charge for their products is not based on R&D costs. The Office of Health Economics in the United Kingdom, that is partly financed by the pharmaceutical industry, looked at R&D costs of developing a new drug in a number of different therapeutic classes and came up with a range of $616 million for HIV/AIDS to $1,203 million for rheumatoid arthritis, i.e., about a 2-fold difference [7]. However, the annual cost for a representative drug, all introduced at roughly the same time, in each of these classes ranged from $560 for asthma to $49,920 for breast cancer, i.e., an 89-fold difference.

Comparison between R&D costs and annual drug costs

Therapeutic class	Average R&D cost for a drug in the class (US$ millions)*	Approximate annual cost of a drug in the class (CAN$)§	Year drug approved in Canada
Rheumatoid arthritis	1,203	17,330 (infliximab)	2001
Alzheimer's disease	1,161	1,710 (memantine)	2004
Asthma	951	560 (montelukast)	1998
Breast cancer	784	49,920 (trastuzumab)	1999
HIV/AIDS	616	7,930 (darunavir)	2006

* Mestre-Ferrandiz et al.
§ Prices from provincial formularies from 2015

The difference in annual cost is clearly not related to the amount spent on R&D but appears to be tied much more to the seriousness of the condition that the drug is designed to treat. Were these drugs highly effective then that difference might be justifiable but for all new cancer drugs for solid tumours introduced between 2002 and 2014, the median gain in overall survival was a modest 2.1 months. Specifically for breast cancer, the best increase in survival was 4.2 months with ado-trastuzumab emtansine for HER2-positive metastatic disease and changes in overall survival were not known for 3 of the 10 new breast cancer drugs [8]. While 4.2 months can clearly be a meaningful amount of time for a woman near the end of her life, it also seems clear that the prices being charged for the drugs are not commensurate with their therapeutic value. Drugs are being priced based on how desperate patients are, not how much it costs to develop them.

Finally, the price should also take into consideration the length of market exclusivity that brand-name products enjoy, i.e., the time between when they are marketed and when a generic competitor appears. Innovative Medicines Canada, the body representing the research-based industry in Canada, claims that market exclusivity in Canada is 8-10 years [9]. I have analyzed the market exclusivity time of the 121 top selling drugs by dollar value from 2009 to 2015. Sixty-three of these drugs were on the market for an average of 12.3 years before a generic competitor appeared and of the 58 without a generic competitor the median time that they had been on the market was 14.7 years [10].

Utilizing pharmacoeconomic evaluations in setting prices

Basing the price on a pharmacoeconomic evaluation is a positive step but utilizing this measure needs to go beyond what is currently in the discussion document. Right now, the PMPRB regulations allow a new drug in an existing class to be priced to the level of the highest priced drug in that class. Brand-name prices do not drop when generic competitors are introduced [11]. By not lowering prices of brand-name drugs, companies thereby enable new entrants into the same therapeutic market to charge higher prices. Drug companies take advantage of this opportunity and almost invariably price their new products to the maximum that is allowed [12]. If new patented drugs do not offer a therapeutic advantage over existing drugs in the same class then, they should be priced at the level of the least expensive generic in the class. Incremental price increases over the generic price should reflect incremental value over the generic.

2. Amending the list of countries used for international price comparisons

The discussion document outlines three factors that were taken into account when choosing the new countries: consumer protection, economic standing, pharmaceutical market characteristics. The proposed new countries are: Australia, Belgium, Japan, Netherlands, Norway, South Korea and Spain. However, according to the PMPRB's own figures drug prices, compared to Canada, are above the OECD average in four out of these seven countries [13]. Eliminating the United States and Switzerland from the reference countries will help bring down Canadian prices but more could be done by choosing a different mix of reference countries, e.g. instead of Japan and Spain using Finland and the Czech Republic that have about the same GDP per capita [14].

Average foreign-to-Canadian price ratios, patented drugs, OECD, 2015 & GDP per capita, 2014

Country	Price ratio compared to Canada	GDP per capita US dollars (000)
United States	2.57	54.4
Mexico	1.07	17.8
Canada	1.00	44.1
Germany	0.99	45.0
Switzerland	0.99	57.2
Japan	**0.91**	**36.5**
New Zealand	0.89	36.8
Sweden	0.89	45.2
Austria	0.88	46.2
Chile	0.86	22.3
Ireland	0.83	46.7
United Kingdom	0.82	39.7
Finland	0.82	40.0
Italy	0.81	35.0
Australia	**0.79**	**45.0**
Belgium	**0.78**	**42.8**
Spain	**0.78**	**33.2**
France	0.78	38.9
OECD median	0.78	38.9

Hungary	0.75	24.7
Netherlands	**0.75**	**47.6**
Luxembourg	0.74	97.3
Norway	**0.73**	**64.8**
Slovakia	0.73	27.7
Poland	0.72	28.4
Slovenia	0.72	30.0
Portugal	0.69	28.4
Greece	0.65	26.0
Estonia	0.64	26.9
Czech Republic	0.62	30.4
South Korea	**0.50**	**34.4**
Turkey	0.38	19.0

3. Reducing regulatory burden for generic drugs with a patent

There is generally a significant difference in the number of violations found between waiting for a complaint and pro-active monitoring. Waiting for complaints about the prices of patented generics risks missing instances where generic prices exceed what is allowed.

The PMPRB should also have the power to deal with situations where the brand name product is no longer being made available and there is a single source for the generic. In this situation since there is no reference brand product there is no control over the generic price.

4. Modernizing reporting requirement for patentees

The current regulations already give the PMPRB the power to require patentees to take other factors into account when determining the introductory price of a new patented medications. The PMPRB should require the submission of the research and development and manufacturing costs.

5. Providing information related to third party rebates

Publicly available prices in other countries frequently do not reflect what is actually paid in those countries. Besides having to provide the PMPRB with discounts and rebates to domestic third-party payers, patentees should also be required to submit prices charged net of discounts or rebates in other countries otherwise the Canadian price will be tied to the price point that is the start of negotiations for other countries.

I would be happy to discuss these issues in greater length with the PMPRB.

Sincerely

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