

Submitted by the Health Charities Coalition of Canada

# Protecting Canadians from excessive drug prices

## Proposed amendments to the Patented Medicines Regulations

Submitted to: Patented Medicines Regulations Consultations  
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June 28 2017

## **EXECUTIVE SUMMARY**

The Health Charities Coalition of Canada is pleased to provide patient-focused input into the proposed amendments to the *Patented Medicines Regulations*. Access to medicines is an important issue for our members and to the Canadians that they serve. Prescription drugs can manage conditions, cure disease(s), improve quality of life, shorten or prevent time spent in hospitals and reduce the demand for health care services, potentially leading to positive health outcomes and decreased costs to the healthcare system. Effective and sustainable regulation of pharmaceuticals is key in being able to provide timely access to medicines for Canadians. It is understood that this consultation is specific to the issue of pricing however, pricing is one piece of a large system that must be addressed in concert with other factors. One cannot address affordability of medicines without also examining availability and accessibility.

HCCC is looking for sustainable change to the regulation of pharmaceuticals in Canada. As this is the first time in twenty years that the Regulations will be updated, we want to ensure that the Regulations are revised in a manner that allows for the further evolution of access to prescription medicines in Canada. For example, ensuring that the Regulations allow for modifications to account for the inclusion of real world evidence and are supportive of the shifts in the health environment. A major change in the healthcare environment has been the move to integrate patient partnerships as a key component of healthcare reforms. HCCC recommends that the PMPRB establish a formal mechanism for meaningfully and continuously engaging patient representatives in their decision making and regulatory processes through patient voice, patient choice, and representation. Additionally, HCCC recommends that any updates to the Regulations be undertaken in a fully transparent manner that; clearly details the nature of the changes, provides all relevant information publicly, includes patients, provides sufficient time for stakeholder input and ensures the continuity of the regulatory approach for patients during the next twenty years. With respect to the current consultation, HCCC provides comment on the following sections:

- With regards to the proposed pharmacoeconomic factors, the QALY evaluation does not include some metrics that are important to patients, the lived experience. HCCC recommends a system in which patient outcomes and quality of life are included as an integral part of any assessment that determines the ceiling price on medications. Additionally, the proposed factors should only be used if they are *complementary* to the HTA evaluation conducted by CADTH, INESSS or other provincial HTA evaluators, not in addition to those processes.
- HCCC is concerned about the limited focus on the size of market use in determining whether or not a drug is priced excessively. The size of market is an important consideration for those launching a new active substance (NAS) in Canada. However, the needs of patients should also be considered, given that they are the primary consumers of the product. Patients' needs and choice must be considered in addition to the analysis of the market in this consultation.
- The proposed list of countries used for international price comparisons, should be evaluated in advance to ensure that their inclusion will not delay launch times in Canada, does not affect Canada's launch standing internationally, and the selected comparator



countries should have comparable health systems overall to Canada's (i.e. language, price lists, etc.).

Canadians deserve high-quality therapies and services that are appropriate for patient needs, respect an individual's choice, and are delivered in a manner that is timely, safe and effective according to the most current evidence available. The review of the PMPRB regulations is an important part of updating Canada's healthcare system. The PMPRB is encouraged to conduct this review in a transparent manner and the Government of Canada is encouraged to communicate to Canadians a greater understanding of how these changes will play into a larger federal government roadmap for making prescription medications more affordable, accessible, and appropriately prescribed.

### **HCCC MEMBER ORGANIZATIONS INVEST IN THE DEVELOPMENT OF NEW MEDICINES**

The Health Charities Coalition of Canada is pleased to provide patient-focused input into the proposed amendments to the *Patented Medicines Regulations*. This submission provides background on how our members invest in the development of new medicines, our general position on access to medicines, and sets out perspectives on certain of the proposed reforms to the Patented Medicine Prices Review Board (PMPRB) and *Patented Medicines Regulations* that govern its work.

The Health Charities Coalition of Canada (HCCC) is a member-based organization comprised of 27 national health charities which represent the voice of patients at all levels of the health continuum. The health charities that HCCC represents strengthen the voice of Canadians, patients and caregivers, and work with others to enhance health policy and increase investment in health research. HCCC strives to ensure that the federal government and policy makers look to the Coalition and its members for timely advice and leadership on major health issues of concern to Canadians; and that they recognize the expertise, commitment, and contributions of health charities in improving the health and well-being of Canadians.

Our members are co-funders, with governments of some of the most important leading health research in Canada. Together we translate knowledge gathered through research to advocate for better public policy and better health outcomes for Canadians. Members of HCCC invest more than \$155 million dollars annually in health research. The members fund leading science in Canada that contributes to the discovery of new medicines.

### **HCCC'S POSITION ON ACCESS TO MEDICINES**

Access to medicines is an important issue for HCCC members and to the Canadians that they serve. Prescription medications can manage conditions, cure disease(s), improve quality of life, shorten or prevent time spent in hospitals and reduce the demand for health care services, potentially leading to positive health outcomes and decreased costs to the healthcare system. Effective and sustainable regulation of pharmaceuticals is key in being able to provide timely access to medicines for Canadians.

Canadians should have equitable access to a comprehensive range of evidence-based medications to meet their respective health care needs. In Canada, public drug plan expenditures were the largest component of prescription medication purchases in 2014. The total that

Canadians paid for prescription medicines that year was \$29.4 billion, 42.6% of which was reimbursed by public drug plans, 35.2% was paid by private plans, and 22.2% was paid out-of-pocket by individuals.<sup>i</sup> Given the current patchwork of pharmaceutical coverage in Canada, cross comparisons between jurisdictions are difficult to make with regards to the individual public drug plans.<sup>ii</sup>

Unfortunately, Canada is not on par with other developed nations when it comes to providing timely, equitable and publicly-funded access to new treatments. The proportion of new medicines that are reimbursed publicly by most drug programs in Canada is in the lower tier of comparable countries, and the time to reimbursement for 80% of the public drug plan beneficiary population is 462 days, ranking Canada 16<sup>th</sup> out of 18 comparable countries.<sup>iii</sup>

The impact of lack of access to needed prescription medications is significant, with low-income Canadians disproportionately affected. While some Canadians can't afford their prescriptions because they have no medication coverage, even patients with insurance can experience financial barriers when they must pay deductibles and co-payments.<sup>iv</sup> It is understood that this consultation is specific to the issue of pricing however, pricing is one piece of a large system that must be addressed in concert with other factors. One cannot address affordability of medicines without also examining availability and accessibility.

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*HCCC Position Statement – Access to Medicines*

*All people living in Canada should have equitable and timely access to necessary prescription medications based on the best possible health outcomes rather than the ability to pay.*

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## **CONTEXT – UPDATING THE REGULATIONS**

Updating the *Patented Medicines Regulations* is welcomed and timely given the focus on innovation and the evolution of Canada's patient population, as there are now 5.9 million Canadian seniors, compared to 5.8 million Canadians who are younger than 15-years-old.<sup>v</sup> HCCC applauds Health Canada and the PMPRB for their desire to modernize the twenty-year-old Regulations with a view to ensuring that effective and relevant regulatory tools are in place to continue protecting Canadians from excessive prices for patented medications. **HCCC recommends that the Regulations be revised in a manner that would allow for the continued introduction of innovative medicines in Canada and be responsive to:**

- *Allow for modifications to account for real world evidence*

Real world evidence can be defined as data used for decision making that are not collected in conventional controlled randomized trials.<sup>vi</sup> The heterogeneity of current pharmacoeconomic methodologies that are typically relied upon by decision-makers which make integrating patient-reported outcomes in the real world challenging. Randomized control clinical trials are an

important aspect of measuring efficacy in limited populations however, they are conducted in an idealized environment and may not factor in important real-life considerations such as compliance, adherence, and convenience. As a result, **any changes made to the Regulations should allow for a flexible framework that would permit the integration of real life evidence as an integral part of the assessment.**

- *Shifts in treatment patterns such as the emergence of precision medicine*

The current health system, and the product assessment tools we rely on to evaluate new treatments, are designed for population health-level determinations, however, advances in medicine such as progress in stem cell research and in innovative treatments such as biologics means that we are much closer to being able to tailor treatments to an individual's unique needs. Precision medicine is one example of a shift in the healthcare environment that demand flexibility be created within the entire medication review and approval process in Canada in order to ensure that patient needs for the most innovative treatments can be met.

The following case study is an example of why the Regulations must be made more flexible. Cystic Fibrosis Canada, in collaboration with the Cystic Fibrosis Foundation in the United States, funded research studies that led to the discovery of cystic fibrosis transmembrane conductance regulator (CFTR) – the “cystic fibrosis gene.” This research identified the structure and function of the protein and its role in the disease, which has led to the

subsequent development of an innovative treatment called KALYDECO™.<sup>vii</sup> The medication has been approved in Canada since 2013, yet has only recently been approved for reimbursement by public drug plans, and in highly restrictive circumstances. Patients expressing most mutations of the gene are ineligible for public coverage despite Health Canada approval of the medicine in treating those patients. This example demonstrates how important it is that **any amendments to the Regulations must be flexible to meet health care needs of individual patients.**

#### *Pharmaceutical Regulation in Canada*

Each agency involved in the regulation of pharmaceuticals in Canada fulfills a key function and we support the unique role that the PMPRB plays in setting the ceiling price for the sale of patented medicines in Canada. Under the current process, Health Canada is responsible for determining market approval and has oversight for product safety, effectiveness and quality. Health technology assessments (HTAs) are conducted by the Canadian Agency for Drugs and Technologies in Health (CADTH) for most of the country and the Institut national d'excellence en santé et en services sociaux (INESSS) in the province of Québec. They determine the clinical

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*“It is widely recognized that the way we approach the understanding, diagnosis, and treatment of disease is rapidly changing. Emerging technologies in genomics, epigenomics, proteomics, nanotechnology, molecular diagnostics and imaging are enabling this rapid revolution. Consequently, there is a growing need to transform from a reactive, one-size-fits all approach to a more personalized system of predictive, preventive, and precision healthcare that is tailored to a population or an individual.”*

-Canadian Institutes of Health Research  
Personalized Medicine Initiative

Retrieved from <http://www.cihr-irsc.gc.ca/e/43627.html> on June 25 2017

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and cost effectiveness of innovative medications and make recommendations about its funding. After those medicines are recommended for reimbursement, the pan-Canadian Pharmaceutical Alliance (pCPA) is responsible for negotiating the cost of the treatment, and finally individual drug plans make the determination about whether or not to list the medication on their formulary. **With these roles in mind, HCCC recommends that no duplication be accepted regarding the respective actions and evaluations followed by each of the various organizations involved in the Canadian medication review and regulation process.**

### **HCCC Recommendation(s)**

- That the Regulations be revised in a manner that would allow for the continued introduction and evolution of innovative medicines in Canada and would be responsive to;
  - Allow for *modifications to account for* real world data
  - Shifts in *treatment patterns* such as the emergence of precision medicine
  - Meet the health care needs of individual patients
- That no duplication be accepted regarding the respective actions and evaluations followed by each of the various organizations involved in the Canadian medication review and regulation process.

### *Patient Partnerships*

A major change in the healthcare environment has been the move to integrate patient partnerships as a key component of healthcare reforms. In the report “Unleashing Innovation: Excellent Healthcare for Canada,” special emphasis is given to patient partnerships and public empowerment.<sup>viii</sup> Patients bring a “lived experience” to the table and are uniquely positioned to provide input and solutions from the perspective of the end-user. Increasingly, patient partnerships are being developed and applied at the individual, organizational and system levels. **HCCC recommends that the PMPRB establish a formal mechanism for meaningfully and continuously engaging patient representatives in its decision making and regulatory processes to ensure patient voice, choice, and representation.**

### **HCCC Recommendation(s)**

- *That the PMPRB establish a formal mechanism for meaningfully and continuously engaging patient representatives in its decision making and regulatory processes to ensure patient voice, choice, and representation.*

### *Transparency*

Patient groups are pleased to provide input into this important consultation regarding proposed changes to the regulations that may have an effect on the medicines that they are taking either through direct costs or through related issues affecting availability and accessibility to medicines. The public release of pertinent data and evidence collected by the Government of Canada related to the assessment and determination of the proposed factors, such as; the criteria and rationale for inclusion in the selection of proposed countries as well as evaluations of international practices would enhance meaningful engagement in this consultation. **It is recommended that the Government of Canada provide patients with relevant knowledge to help them make informed decisions regarding input into future submissions before any changes are made.**



Additionally, the Government of Canada is encouraged to communicate to Canadians a greater understanding of how these changes will play into a larger federal government roadmap for making prescription medications more affordable, accessible, and appropriately prescribed.

Moving forward, **HCCC recommends that any updates to the Regulations be undertaken in a fully transparent manner** that; clearly details the nature of the changes, provides all relevant information, includes patients, provides sufficient time for stakeholder input and ensures the continuity of the regulatory approach for patients during the next twenty years.

### ***HCCC Recommendation(s)***

- That the Government of Canada provide patients with relevant knowledge to help them make informed decisions regarding input into future submissions before any changes are made.
- Updates to the Regulations must be undertaken in a fully transparent manner.

## **INPUT ON SPECIFIC PROPOSED REFORMS**

### **Introducing new factors to help determine whether a price is excessive**

All Canadians should have equitable access to a comprehensive range of evidence-based medications to help meet their health needs, regardless of who they are, the setting they are in, or where they live in Canada. **HCCC recommends that any current or proposed factors used to regulate excessive medication pricing in Canada should be complementary to the existing regulatory mechanisms, such as HTA processes.** The proposed factors should only be used if they are *complementary* to the HTA evaluation conducted by CADTH, INESSS or other provincial HTA evaluators, not in addition to those processes. **The important role and relevance of HTA reviews should not be duplicated by the PMPRB.**

**Also, any changes made to the Regulations should not have a negative effect on the overall length of time for medications to reach Canadian patients.** Canadians suffer when they wait too long and/or are denied coverage for new evidence-based medicines to treat their respective conditions or disorders. For example, a recent study to determine the average time from Health Canada approval to provincial reimbursement in Ontario and Quebec for novel oncology drugs found that the median time from notice of compliance, to provincial listing was 382 days in Ontario and 367 days in Quebec.<sup>ix</sup> Living with a diagnosis is difficult, knowing that that there is a treatment that has been approved, yet is unavailable to you, can be unbearable.

### *Pharmacoeconomic evaluation for the medicine*

The notion that pharmacoeconomic assessments can be utilized to assess the excessiveness of a given price may be attractive conceptually. However, the reliance on these comparative cost-effectiveness techniques could be problematic for a number of reasons.

First, the assessment of cost per Quality Adjusted Life Year (QALY) is dependent upon assumptions that can vary broadly, meaning that small adjustments in assumptions could create large variations in the end result. For example, manufacturers often present different assumptions (such as the prevalence of a disease) from those relied upon by CADTH.

In addition, the QALY-based evaluation does not account for some important metrics to patients, such as the frequency of taking the medication and/or the delivery mechanism (oral/injectable etc.), and side effects of taking the medication.

The subjectivity of QALYs is often debated as well. This measure does not always capture all of the benefits of a healthcare intervention, in this case, medicines. Often, it is assumed that all QALYs are representative of the same societal value of quality of life. This risks ignoring the equity concerns of individual patients.<sup>x</sup> In a country and political climate that strives to support the middle class, a utilitarian approach should be closely examined so that patient populations, whether small or large, should not have to sacrifice their own well-being for the greater good of the collective.

Often QALYs do not capture the positive effects that an innovative medication offers to a given patient. For example, a patient who is successfully being treated early and effectively with a medication would be able to return to work and not make as frequent trips to the hospital. Rather than just the quantitative analyses, the qualitative, lived experience of patients should be taken into consideration in decision-making.

Another area of concern is the impact that this proposed change could have on people with rare diseases. Generally, **QALY analyses do not have favourable outcomes for patients who need rare disease medicines, known as orphan therapies. Using this methodology, orphan therapies are typically found to be “cost-ineffective” and lacking in long-term data on safety and effectiveness relative to other conditions and diseases. These results are misleading and reflect a systemic limitation of the methods, rather than the medications. It must be kept in mind that the practice of medicine changes over time.** For example, transplants were met with resistance historically since they were considered “radical” and “expensive,” but now they are considered standard practice.<sup>xi</sup> As it is, Canadian patients with rare diseases face disadvantages given that their treatments are often deemed too “expensive” by our current HTA review process. If the PMPRB relies on the same tools, the ceiling price could be expected to be set at a level which could make access and availability even more difficult for patients than is currently the case.

### ***HCCC Recommendation(s)***

- HCCC recommends that any factors that are used to regulate excessive medication pricing in Canada should be complementary to the existing regulatory mechanisms, such as HTA processes. The important role and relevance of HTA reviews should not be duplicated by the PMPRB.
- Any changes made to the Regulations should not have a negative effect on the overall length of time for medications to reach Canadian patients.
- Any analysis of the value of a medication for pricing purposes should reflect the full value of the treatment to individual patients and the healthcare system.
- The Regulations include provisions to ensure that Canadians with rare diseases are not further disadvantaged.

*The size of market for the medicines in Canada and in countries other than Canada*



**HCCC is concerned about the limited focus on the size of market use in determining whether a medication is priced excessively.** The size of market is an important consideration for those launching a new active substance (NAS) in Canada. However, the needs of patients should also be considered, given that they are the primary consumers of the product. Patients' needs and choice must be considered in addition to the analysis of the market in this consultation.

**Many Canadians face barriers in accessing the therapies they need. Any analysis of the market by PMPRB must consider that a given medication may not meet the needs of all patients living with that respective disease or disorder.** See the example below from the Multiple Sclerosis Society of Canada:

*“There is no ‘standard’ MS medication. Although several MS medications have similar mechanisms of action, dosing and administration are not the same and therefore the options available to people are selected based on tolerance, known (expected) side-effects, lifestyle choices, disease course and cost. It is common for one treatment to work well in one individual, and fail in another.*

*Health Canada has approved eleven drugs to treat relapsing forms of MS, collectively referred to as disease-modifying therapies, or DMTs. The annual cost of DMTs range from approximately \$16,000 to \$30,000 for first-line therapies, and \$50,000 or more, for second or third line therapies. The vast majority of these drugs are included on provincial, territorial and federal formularies, overseen by ‘special’ or ‘exceptional access’ drug programs that require a case-by-case approval for reimbursement due to their high cost. Certain criteria must be met in order for a specific patient to be eligible for public reimbursement or coverage of these drugs.”*

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The above example highlights the diverse needs of patients in Canada. There may be more than one treatment in one class that could prove to be the optimal choice for a patient. Moreover, there are often situations which require the patient to switch from one therapy to another when the first no longer offers the same results. Ensuring a range of effective choices are available is vital.

It is unclear how the size of market will be taken into account when determining excessive pricing. In comparing other market sizes, is the proposal only to examine countries that are listed as comparator countries or to expand beyond? How will factors such as prevalence and cost effectiveness weigh in the determination of pricing? In absence of a clear understanding of the proposal to examine market size, we are unable to provide additional feedback on this new factor.

### **HCCC Recommendation(s)**

- In addition to market size considerations, the needs of patients should also be taken into account.
- Any analysis of the market by PMPRB must consider that one medication may not meet the needs of all patients living with that respective disease or disorder.

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

With respect to the schedule of comparator countries, HCCC makes the following recommendations:

First, **that any amendments to the Regulations must be evaluated in advance to ensure that their inclusion will not delay launch times in Canada.** According to a National Prescription Drug Utilization Information System analysis of the PMPRB7 (France, Germany, Italy, Sweden, Switzerland, United Kingdom, and the United States), Canada's weighted average lag time - the number of months from the first launch in any of the markets analyzed to the launch in a particular country – was eight months and the median was 11 months. This result was similar to Switzerland and shorter than France and Italy, but longer than in the US, the UK, Sweden and Germany.<sup>xiii</sup> Clearly then, Canada is not currently an international leader regarding market launch times.

HCCC's second recommendation is **that the PMPRB ensure any changes to the schedule of comparator countries does not affect Canada's launch standing internationally.** Canada's health care standards are quite high. As such, any countries included in the schedule should have a similar standard of health care as Canada. Also, as part of the comparison and analysis process, patient access should be considered as a key factor. Given that many patients receive innovative medicines in Canada through clinical trials, policymakers should consult international comparator countries and consider the impact of the changes on access to clinical trial medications and international differences in clinical trial performance on launch dates.

HCCC's final suggestion is to recommend **that selected comparator countries should have comparable health systems overall to Canada's.** In that regard, the following system elements should be considered: language, price, general medical practices, and systems regulations. These suggestions could be a frame of analysis when considering the list of countries which could be reasonably compared to Canada. For example, ensuring that the sources of information and language used in the analysis are comparable (i.e., the same price list), or how medicines are prescribed and distributed to patients. Ideally then, any analysis of relevant comparator countries would take account of **how medications reach patients**, which includes the considerations of affordability, access, and appropriate prescribing.

#### ***HCCC Recommendation(s)***

- Any amendments to the Regulations must be evaluated in advance to ensure that their inclusion will not delay market launches in Canada.
- The PMPRB should ensure that any changes to the schedule of comparator countries does not affect Canada's launch standing internationally.
- Selected comparator countries should have comparable health systems overall to Canada's.

#### **Providing information related to third party rebates**

It is unclear to HCCC what role the reporting of manufacturer rebates is intended to have on the PMPRB pricing review process, or the rationale behind requiring such reporting, so it is difficult to comment precisely on the proposal. The practice of manufacturers offering confidential financial concessions to public payers in the context of national product negotiations has resulted in improved access to publicly funded medications in recent years. The concern is that new reporting requirements could potentially motivate those manufacturers to desist from doing so, or reducing the value of those concessions. **Before introducing such a reporting requirement, it would be important to establish what the implications of that action might be on the marketplace,**

and care must be taken to ensure that it does not result in less access to needed medications for patients.

## **CONCLUSION**

Canadians deserve high-quality therapies and services that are appropriate for patient needs, respect an individual's choice, and are delivered in a manner that is timely, safe and effective according to the most current evidence available. The review of the PMPRB regulations is an important part of updating Canada's healthcare system.

The Health Charities Coalition of Canada is pleased to provide comment, and looks forward to continued discussion on the availability and access to medicines for Canadians as one discussion cannot happen in isolation of the other. We would be pleased to meet with you to further discuss any of our recommendations.

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<sup>i</sup> Patented Medicine Prices Review Board. (May 2017). *CompassRx, 3rd edition: Annual Public Drug Plan Expenditure Report, 2015/16*. Canada: Ottawa. Retrieved from: <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1314>

<sup>ii</sup> *Ibid*, p. 5

<sup>iii</sup> Rx&D. (2015). "Access to New Medicines in Public Drug Plans: Canada and Comparable Countries, Annual Report." Retrieved from: [http://stream1.newswire.ca/media/2015/05/21/20150521\\_C8665\\_PDF\\_EN\\_16843.pdf](http://stream1.newswire.ca/media/2015/05/21/20150521_C8665_PDF_EN_16843.pdf)

<sup>iv</sup> *Ibid*.

<sup>v</sup> Statistics Canada. (2016). *Census of Population, Age and Sex Highlight Tables*. Canada: Ottawa

<sup>vi</sup> Garrison, L.P. et. Al. (2007). "Using real world data for coverage and payment decisions: the ISPOR real world data task force report," *International Society for Pharmacoeconomics and Outcomes Research*. Retrieved from: [https://www.ispor.org/workpaper/RWD\\_TF/RWTFManuscript.pdf](https://www.ispor.org/workpaper/RWD_TF/RWTFManuscript.pdf)

<sup>vii</sup> Cystic Fibrosis Canada. (2017). *About our Research*. Retrieved from: <http://www.cysticfibrosis.ca/our-programs/research/about-our-research>

<sup>viii</sup> Health Canada. (July 2015). *Unleashing Innovation: Excellence for Healthcare in Canada, Report on Advisory Panel on Healthcare Innovation*. Canada: Ottawa. Retrieved from: <https://www.canada.ca/content/dam/canada/health-canada/migration/healthy-canadians/publications/health-system-systeme-sante/report-healthcare-innovation-rapport-soins/alt/report-healthcare-innovation-rapport-soins-eng.pdf>

<sup>ix</sup> Bremner, S. & et. Al. (May 2017). *Average Time to Patient Access from Drug Approval: An Analysis of Ontario & Quebec, QuintilesIMS*. Poster presented at the ISPOR 2<sup>nd</sup> Annual International Meeting, May 20-24, 2017. Boston, MA, USA. Retrieved from: <http://imsbrogancapabilities.com/pdf/rwe/qi-isp-or-boston-poster.pdf>

<sup>x</sup> Whitehead, S. J. & A. Shehzad. (2010). "Health outcomes in economic evaluation: the QALY and utilities," *British Medical Bulletin*. 96: 5-21. DOI:10.1093/bmb/ldq033

<sup>xi</sup> Hyry, H.I. et. Al. (2014). "Limits on use of health economic assessments for rare diseases," *International Journal of Medicine*, 107 (3): 241-245. doi: 10.1093/qjmed/hcu016. Retrieved from: <https://academic.oup.com/qjmed/article/107/3/241/1570371/Limits-on-use-of-health-economic-assessments-for>

<sup>xii</sup> Multiple Sclerosis Society of Canada. (2016). *Feedback submitted to the Patented Medicines Price Review Board from the Multiple Sclerosis Society of Canada related to Excessive Drug Pricing in Canada*. Retrieved from: [http://www.pmprb-cepmb.gc.ca/CMFiles/Consultations/Rethinking\\_the\\_Guidelines\\_2016/Submission\\_MS\\_Society\\_of\\_Canada\\_Oct\\_2016.pdf](http://www.pmprb-cepmb.gc.ca/CMFiles/Consultations/Rethinking_the_Guidelines_2016/Submission_MS_Society_of_Canada_Oct_2016.pdf)

<sup>xiii</sup> Patented Medicine Prices Review Board. (April 2017). *Meds Entry Watch, 2015*. Canada: Ottawa. ISSN 2560-6204, p. 11. Retrieved from: <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1307>