

Rogue Regulator

PMPRB's false narrative is driving
dangerous drug price controls



Brett Skinner PhD

Rogue Regulator

PMPRB's false narrative is driving dangerous drug price controls

Brett Skinner PhD

© Canadian Health Policy Institute Inc. 2021

ISSN 2562-9492

<https://doi.org/10.54194/YQYB2454>

www.canadianhealthpolicy.com

Table of Contents

PREFACE4

CHAPTER 1: INTRODUCTION6

CHAPTER 2: PRICE CONTROLS10

INTERNATIONAL PRICE REFERENCING10

PHARMACOECONOMIC VALUE ASSESSMENT (PVA).....15

NET CEILING PRICES.....17

REGULATORY IMPACT ON PRICES.....20

CHAPTER 3: PRICE AND NEW DRUG LAUNCHES21

CHAPTER 4: PRICE AND INDUSTRY-FUNDED PHARMACEUTICAL R&D24

CHAPTER 5: PRICES FOR PATENTED MEDICINES31

PRICES IN THE PMPRB733

PRICES IN 14 PMPRB COUNTRIES.....35

CHAPTER 6: PATENTED MEDICINES EXPENDITURE (PMEX)38

CHAPTER 7: COST V BENEFITS43

CHAPTER 8: ROGUE REGULATOR.....49

FALSE NARRATIVE, RISKY REGULATION.....49

PUBLIC ACCOUNTABILITY AND THE DUTY OF NEUTRALITY.....50

ABOUT THE AUTHOR53

REFERENCES.....54

Preface

There is a consensus among economists that government price controls are generally ineffective at achieving their intended purpose, tend to distort the allocation of resources, and often produce inequitable social outcomes.¹ It is also widely observed by economists that price regulation depresses pharmaceutical innovation, which affects health outcomes, resulting in higher expenditures on other forms of medical care.^{2,3} Economists generally agree that efficient spending on health is an investment in human capital which is a contributing factor to economic productivity, and that pharmaceutical innovation has been a major contributor to better health outcomes, improved quality of life, and longer life expectancy.⁴

So why is the federal government imposing extreme price regulations that will discourage drug-makers from launching new innovative medicines and investing in pharmaceutical research in Canada?

In January 2022, the government is introducing new price control guidelines at the request of the federal regulator known as the Patented Medicine Prices Review Board or PMPRB. The regulator estimated the changes will cut Canadian prices for patented medicines by more than half the current level. That would make our prices the lowest in the world.

Since 2015, the agency has run a communications campaign to justify the amendments, raising alarms about high prices for patented medicines and the impact on healthcare costs. At the same time, it has insisted that the changes will not reduce the availability of new medicines or impact industry investment in pharmaceutical research in Canada. In a 2020 article, the Executive Director of the PMPRB wrote “there is no evidence of a link between pricing, research and development, and access to medicines”.⁵

It is hard to believe that mandatory price cuts of such severe magnitude won't negatively impact industry decisions about whether Canada is a priority market for new therapeutic products, or whether it is the best place to spend scarce research dollars. The government is wrongly assuming that the industry will continue to prioritize our market at any price decreed by the PMPRB.

The government is also not thinking about how long it took to build the clinical science infrastructure in Canada. The regulations risk eroding valuable

institutional knowledge and technical expertise, and it will be expensive to restore.

The truth is the regulator is aware of evidence that contradicts its narrative justification for amending the regulations but seems to have chosen to suppress it. Moreover, PMPRB has not provided parliament with any evidence to support its narrative.

In this book I review some of the evidence the PMPRB said did not exist. I also discuss the rogue behavior of the agency.

The Government is making these changes based on advice from a regulator that has a conflict of interest. The PMPRB not only initiated the regulatory changes, but also wrote the new rules, self-evaluated the impact on prices, managed public consultations, and controlled the flow of information to parliamentarians.

Important stakeholders and prominent academics have raised questions about the PMPRB's commitment to its duty of neutrality as a public agency. The Federal Court of Appeal even criticized PMPRB for bending its own rules, breaching its jurisdiction and for obfuscating behavior, which makes it impossible to review its administrative decisions.

The Parliament of Canada is obligated to reconcile the PMPRB's narrative with the evidence presented in this book. It should conduct a formal review of the agency's relevance. Due consideration should be given to retiring its mandate.

Brett Skinner, PhD

Chapter 1: Introduction

The prices of patented medicines sold in Canada are regulated by a quasi-judicial agency of the federal government known as the Patented Medicine Prices Review Board (PMPRB). In January 2022, the Government of Canada is implementing major changes to the PMPRB, affecting the way drug prices are regulated. The changes are dangerous and unnecessary.

The Board was established as part of the reforms to the Patent Act 1985, which strengthened intellectual property rights protections for pharmaceuticals. The PMPRB was the government's policy response to critics who were concerned that the reforms would allow patent-holders to abuse monopoly pricing power.

It is an independent, arm's-length agency of Health Canada, but is not subject to ministerial direction. The agency reports directly to Parliament. Within the limits of the Act and the Regulations, PMPRB rulings and orders have the same enforceability as the Federal Court. Its regulatory authority applies to all drugs with active patents, and which are sold in Canada, and includes both public sector and private sector sales.

The agency has a mandate to prevent innovative pharmaceutical companies (aka "patentees") from charging excessive prices for patented medicines. The Regulations require the Board to use international referencing to determine whether Canadian prices are excessive. The Board is empowered to assess financial penalties against patent-holders for charging prices that are, in the Board's opinion, excessive. The regulations do not define what "excessive" means. The Board has the freedom to use any reasonable methods to define excessive prices.

The second part of its mandate is to monitor and report on prices for patented drugs. The regulator also reports the research and development (R&D) spending and sales trends of patentees because the federal government strengthened pharmaceutical patents with the expectation that it would attract foreign direct investment in R&D to the country. In exchange for protecting the property rights of patentees, the government expected the industry to spend 10% of its Canadian sales on R&D in Canada.

It is important to note that the PMPRB is an aberration. No other industry in Canada is subject to direct price regulation. Nor is the protection of intellectual

property rights conditional on the R&D to sales ratio for any other business sector. The Board has no international counterpart. No other country regulates drug prices using an agency like the PMPRB.

The pending regulatory changes will make Canada a more extreme outlier because the new rules are more severe than any other regime in the world. Nothing like this has been tried anywhere else.

The upcoming changes were first proposed by the PMPRB in 2015. A long process ensued, which included several public consultations, culminating in the final regulations being announced in August 2019.^{6 7} The new regulations were to come into effect on July 1, 2020, but the government delayed implementation until January 1, 2021, due to the COVID-19 pandemic. In December 2020, the government announced a second delay extending to July 1, 2021. Most recently, in June 2021, the government announced a third delay until January 1, 2022.

The purpose of the regulatory amendments is clear. According to Health Canada, “The Government of Canada is firmly committed to... taking action to significantly **lower the cost of prescription drugs**... This important work includes **reducing the cost of patented drugs through the modernization of the pricing framework under the Patented Medicine Prices Review Board**.”⁸

How will the regulations affect patented drug prices? The federal government’s Strategic Policy Branch estimated that the changes will cut the maximum prices allowed for patented medicines by more than half the current price ceiling.⁹

Industry, patient groups and researchers have warned that the lower price limits could cause pharmaceutical companies to deprioritize the Canadian market when launching new medicines and will delay access to innovative therapies for Canadian patients. They also expressed concerns the new regulations will discourage industry investment in pharmaceutical research and development (R&D) in Canada.

The PMPRB rejects such concerns. Citing a lack of evidence, it stated that “prices do not appear to be an important determinant of medicine launch sequencing” and “The link between high domestic prices and industry investment has not been demonstrated.”¹⁰

Despite the PMPRB’s assertion, there is in fact plenty of evidence. Labrie (2020) conducted a systematic literature review and found 44 peer-reviewed studies

showing that drug price controls reduce the availability of innovative drugs and/or discourage industry investment in pharmaceutical R&D.¹¹

The Government of Canada is wrong to assume that the changes are benign. The new price limits are hostile to innovation and will disincentivize pharmaceutical firms from prioritizing the Canadian market when launching new medicines. Many advanced therapies will likely be available to patients in other countries for years before becoming available to Canadians.

Industry investment in pharmaceutical R&D is driven by multiple variables. There is quite a lot of empirical evidence that the price ceiling for patented medicines is an important factor in company decisions about where to locate industry-funded clinical research. The PMPRB regulatory changes will likely cause a substantial decline in the number of industry-funded clinical trials in Canada.

The amended regulations are not only risky, they are not even necessary. The prices of patented medicines in Canada are not excessive. The truth is, that patented medicines have accounted for a stable, small percentage of national health expenditures (NHEX) and gross domestic product (GDP) for more than 30 years, and Canadian prices for patented medicines fall in the middle of prices in comparable countries, and appropriately reflect the country's GDP per capita.

Indeed, it is reasonable to ask whether Canada needs a federal drug price regulator at all? The PMPRB's relevance is questionable because its function is redundant. Several other agencies are involved in regulating the efficacy and price of new drugs.

Before any new drug can be sold in Canada, it must first be approved by Health Canada, which assesses the safety and therapeutic effectiveness by reviewing published clinical evidence about the drug.

Following successful approval by Health Canada, all new drugs must pass through health technology assessment (HTA) at the Canadian Agency for Drugs and Technology in Health (CADTH), which conducts a review of the evidence regarding the cost effectiveness of the drug using pharmacoeconomic techniques and concepts like cost per quality adjusted life year (QALY). CADTH makes recommendations regarding reimbursement on behalf of all federal and provincial public drug plans, except Quebec which utilizes its own HTA agency

known as the Institut national d'excellence en santé et en services sociaux (INESSS).

Following this, all new drugs are subject to price negotiation with the pan-Canadian Pharmaceutical Alliance (PCPA), which acts as a monopsony purchaser on behalf of every federal and provincial public drug plan. The PCPA negotiates prices that are well below the list prices permitted by the PMPRB.

It is hard to justify the need for a federal price regulator when new drugs are already subject to a complex process of approval and negotiation that results in prices that are lower than the ceiling prices imposed by the regulator. It is increasingly obvious that the PMPRB's mandate is obsolete.

This explains why the regulator so aggressively advocated for the regulatory changes. The PMPRB is engaged in a desperate attempt to preserve its bureaucratic relevance. The analysis presented in this book suggests the PMPRB has used a false narrative to drive dangerous changes to drug price controls in Canada.

In Chapter 2 I briefly describe the pending regulatory changes and offer a critical analysis. In Chapters 3 to 6 I review some of the evidence that the PMPRB has ignored regarding the key elements of its narrative including: the link between price and new drug launches, the correlation between price and industry funding for clinical research, whether prices are too high in Canada, and whether those prices are causing unsustainable costs for the healthcare system. Chapter 7 reviews a small sample of evidence demonstrating the benefit of pharmaceutical innovation, something which too often gets left out of discussions about the cost of patented medicines. Chapter 8 sums up my final thoughts about the rogue behavior of the PMPRB, including its false narrative and its disregard for public accountability and the public service duty of neutrality.

Chapter 2: Price Controls

International Price Referencing

The PMPRB uses international price referencing as one of its methods, to regulate against excessive prices for patented medicines sold in Canada. Under the current regulations, the Canadian price is deemed to be excessive if it exceeds the median international price (MIP) for the same drug sold in a specified group of reference countries.

Known as the PMPRB7, the seven countries currently specified by the regulations for international price referencing to Canada include France, Germany, Italy, Sweden, Switzerland, the United Kingdom, and the United States.

The new regulations change the mix and the number of reference countries used for price comparison. The PMPRB7 expands to the PMPRB11 by removing the United States and Switzerland and adding Australia, Belgium, Japan, Spain, Netherlands, and Norway.

[EXHIBIT 1]

The changes are associated with several problems which the PMPRB has failed to bring to the attention of parliament. First of which is that the new PMPRB11 countries are not an objective comparator group. The PMPRB’s selection of reference countries was arbitrary. To be included, the agency required the countries to be like Canada on the basis of GDP per capita, population, and market entry of new products. The inclusion criteria specified by the PMPRB were inconsistently applied.

Take the GDP per capita criteria for example. Average income varies widely across current and former PMPRB reference countries. This makes it nearly

EXHIBIT 1.

PMPRB reference countries

Canadian price deemed “excessive” if it exceeds the median international price (MIP)

1987-2021	2022-
PMPRB 7	PMPRB 11
USA	USA AUS
UK	UK BEL
GER	GER JPN
FRA	FRA NLD
SWI	SWI NOR
ITA	ITA SPA
SWE	SWE

impossible to exclude any of the former reference countries on the basis of differences or similarities related to GDP per capita.

EXHIBIT 2 shows data sourced from the Organization for Economic Cooperation and Development (OECD) for GDP per capita denominated in US dollars at purchasing power parity (PPP) for each of the seven current and six new reference countries to Canada.

Notice that, in 2020 GDP per capita in the United States (\$63,415) and Norway (\$63,293) was 32% higher than Canadian GDP per capita (\$48,091). Yet the US was excluded, while Norway was included as a reference country.

Inconsistencies in the application of the population criteria are also obvious. Comparing the most recent population data from the OECD [**EXHIBIT 2**] shows Sweden at 10.2 million, Switzerland at 8.5 million, and Norway at 5.3 million. Yet Switzerland was excluded, while Sweden and Norway were included as reference countries.

The United States population (327.1 million) is 9 times larger than Canada (37.3 million), but Canada's population is 7 times greater than Norway. Yet the US was excluded, while Norway was included.

EXHIBIT 2. Population 2019 and GDP per capita
US \$ PPP 2020, PMPRB14

	POP	GDP PC
AUS	25,357,553	\$51,743
BEL	11,455,519	\$52,063
CAN	37,317,904	\$48,091
FRA	67,177,636	\$46,537
GER	83,019,213	\$53,812
ITA	59,816,673	\$41,492
JPN	126,443,180	\$40,150
NLD	17,282,163	\$59,335
NOR	5,328,212	\$63,293
SPA	46,937,060	\$38,335
SWE	10,230,185	\$54,848
SWI	8,544,527	\$71,298
UK	66,647,112	\$44,929
USA	327,170,529	\$63,415

Data: OECD

PMPRB data [**EXHIBIT 3**] show that the US has the highest degree of commonality with Canada regarding the market entry of new drug products. Of the 128 new active substances (NAS) launched in Canada between 2009 and 2014, 123 were also launched in the US. The same data show that of the 128 NAS launched in Canada, 91 were also launched in Switzerland, which is higher

than the 76 NAS launched in France.¹² Yet France was included as a reference country by the PMPRB while the US and Switzerland were excluded.

A quick look at the impact on the MIP from the new PMPRB11 is shown in **EXHIBIT 4**. Using data published by the PMPRB it is apparent that relative to the PMPRB7, the PMPRB11 is overrepresented by lower priced markets. The PMPRB7 group of countries had balanced representation from higher priced and lower priced markets. The exclusion of higher priced markets and the inclusion of additional lower priced markets artificially depresses the MIP. The difference is about 4% according to these data.¹³

Incidentally, it is worth noting that excluding high-price markets from the PMPRB reference countries, undermines the value of the Board’s reporting mandate because it deprives policymakers of vital information about the effect of price regulations on the availability of new medicines, industry investment in clinical research, and the development of an innovative domestic pharmaceuticals industry in Canada. For example, the United States has the highest drug prices in the world, but Americans get the earliest access to new medicines and the country attracts the highest levels of industry investment in research and development of innovative pharmaceuticals. It serves the public interest for policymakers to be informed of this reality and the trade-offs associated with alternative policy approaches.

EXHIBIT 3. New drug launches matching products launched in Canada, 2009 to 2014

NAS LAUNCHED	
Canada	128
United States	123
Germany	111
United Kingdom	105
Sweden	103
Italy	94
Switzerland	91
France	76
Data: PMPRB, NPDUIS	

EXHIBIT 4. MIP PMPRB7 v PMPRB11

	PMPRB7	PMPRB11
AUS		0.70
BEL		0.83
FRA	0.73	0.73
GER	1.02	1.02
ITA	0.91	0.91
JPN		0.93
NLD		0.76
NOR		0.88
SPA		0.89
SWE	0.87	0.87
SWI	1.02	
UK	0.82	0.82
USA	3.49	
MEDIAN	0.91	0.87

Data: PMPRB (source: IQVIA)

However, a more important problem is that international price referencing is a moving target. The position of the MIP, bilateral price ratios and country ranks are sensitive to the data sources and methods used to calculate them. To illustrate this, we can look at some data from a recent study I conducted.¹⁴

The data in **EXHIBITS 5A-5B** are from IQVIA, the same source used by PMPRB for the data in **EXHIBIT 4**. However, the data sample and methods differ from the PMPRB as I explain in Chapter 5.

The data include the average foreign-to-Canadian price ratios in the PMPRB7 and PMPRB11 countries for the patented drugs most likely to exceed the sales threshold triggering a pharmacoeconomic value assessment (PVA), which I describe in the following section. The sample included 100 top selling patented medicines in Canada from 2018 to 2020 and is estimated to represent close to 50% of the total market for sales of patented medicines in each year.

EXHIBIT 5A. MIP at MER				
	PMPRB7			
	2018	2019	2020	2018-20
FRA	0.952	0.880	0.864	0.898
GER	1.180	1.110	1.098	1.129
ITA	1.139	1.140	1.165	1.148
SWE	0.945	0.920	0.912	0.926
SWI	1.088	1.100	1.149	1.112
UK	0.898	0.900	0.891	0.896
US	4.378	4.470	4.319	4.389
CAN	1.000	1.000	1.000	1.000
	PMPRB11			
	2018	2019	2020	2018-20
AUS	0.839	0.770	0.742	0.784
BEL	1.091	1.040	1.037	1.056
FRA	0.952	0.880	0.864	0.898
GER	1.180	1.110	1.098	1.129
ITA	1.139	1.140	1.165	1.148
JPN	0.924	0.970	0.954	0.949
NLD	0.907	0.820	0.793	0.840
NOR	0.946	0.910	0.842	0.900
SPA	1.234	1.180	1.200	1.205
SWE	0.945	0.920	0.912	0.926
UK	0.898	0.900	0.891	0.896
CAN	1.000	1.000	1.000	1.000
Data: IQVIA				

EXHIBIT 5B. MIP at PPP				
	PMPRB7			
	2018	2019	2020	2018-20
FRA	0.985	0.960	0.898	0.948
GER	1.215	1.220	1.147	1.194
ITA	1.319	1.340	1.282	1.313
SWE	0.864	0.880	0.806	0.850
SWI	0.822	0.830	0.781	0.811
UK	0.903	0.940	0.891	0.911
US	4.028	4.240	4.132	4.133
CAN	1.000	1.000	1.000	1.000
	PMPRB11			
	2018	2019	2020	2018-20
AUS	0.698	0.670	0.664	0.677
BEL	1.127	1.110	1.054	1.097
FRA	0.985	0.960	0.898	0.948
GER	1.215	1.220	1.147	1.194
ITA	1.319	1.340	1.282	1.313
JPN	0.911	0.920	0.863	0.898
NLD	0.946	0.860	0.784	0.864
NOR	0.722	0.700	0.707	0.710
SPA	1.480	1.500	1.419	1.466
SWE	0.864	0.880	0.806	0.850
UK	0.903	0.940	0.891	0.911
CAN	1.000	1.000	1.000	1.000
Data: IQVIA				

Bilateral foreign-to-Canadian price comparisons were limited to symmetrical drug molecules with the same domestic patent protection status. The analysis used a standardized unit of measure for calculating foreign-to-Canadian price ratios that is comparable across varied dosage strengths, pack sizes and sales weights: defined as gross sales at manufacturer list prices per standard unit sold.

The median international price in each year is highlighted. Canada's ratio is held constant. Prices are denominated in US dollars at market exchange rates (MER) and at PPP.

The results clearly show significant variance between the estimates of foreign-to-Canadian price ratios. The MIP fluctuates depending on the data source, data sample, method, currency adjustment and year. Notice in **EXHIBITS 5A-5B** that Switzerland flips from a high-cost market to a low-cost market when prices were denominated at PPP versus MER. Note also that the magnitude of the change in MIP associated with the move from PMPRB7 to PMPRB11 reference countries is larger using this method versus the method used in **EXHIBIT 4**.

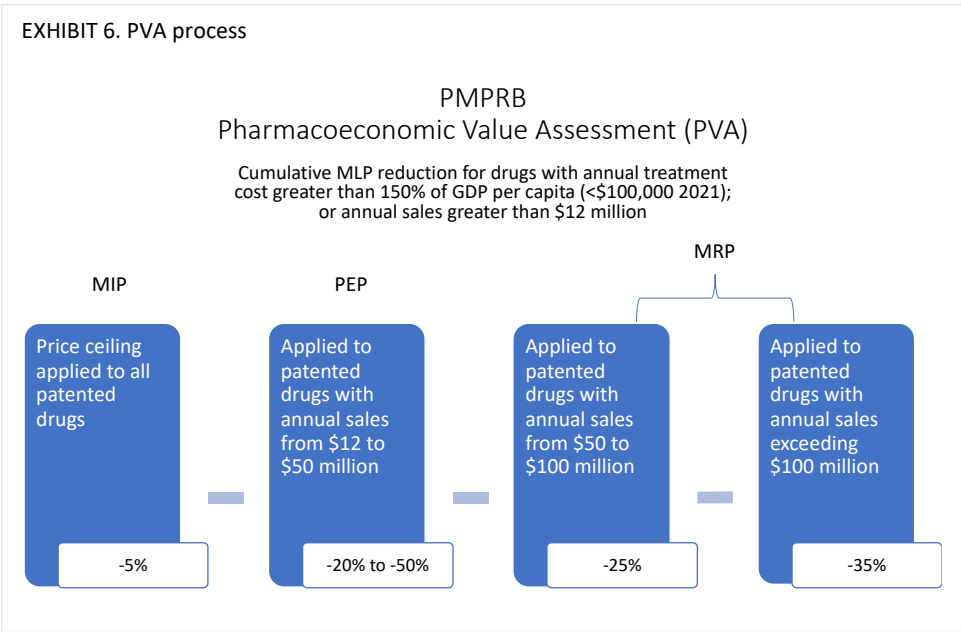
While the regulations specify the countries that the PMPRB must use for price referencing, the agency is pretty much free to use any method it chooses to define excessive prices for the purpose of enforcing regulations. The MIP could be a moving target depending on whether the regulator uses MER or PPP to denominate prices, or a different time period (for example, the most recent year, or the average of the most recent three years), or the average prices of all patented medicines versus a sample of patented medicines that are subject to PVA, etc.

The regulatory metrics are fluid, yet they have the force of law. As I explain further in Chapter 5, there are other limitations associated with the method used by the PMPRB that challenge the objectivity of the regulations. The limitations demonstrate the folly of the notion that regulators can set prices without distorting the market. The use of methods like international price referencing merely provides false scientific legitimacy for what are really just arbitrary rules. As I will discuss in the next section, the same thing can be said about PVA.

Pharmacoeconomic Value Assessment (PVA)

In addition to the PMPRB11 median international price test, the price control guidelines introduce a pharmacoeconomic value assessment (PVA) for new medicines. Patented drugs priced higher than their computed pharmacoeconomic value will be subjected to dramatic price cuts. The regulations also impose profit controls on drug products with sales revenue exceeding defined thresholds.

The price control guidelines pertaining to PVA are very complicated. A simplified illustration of the process is shown in **EXHIBIT 6**. PVA applies to new drugs that have a 12-month treatment cost greater than 150% of GDP per capita. First, a Maximum List Price (MLP) ceiling is set according to the MIP of the PMPRB11 countries. The MLP is reduced to the Pharmacoeconomic Price (PEP) based on the regulator’s assessment of therapeutic benefit, and cost-effectiveness measured as the cost per Quality Adjusted Life Year (QALY) (aka the Pharmacoeconomic Value Threshold, or PVT). The MLP is further reduced for the size of the market, defined by sales revenue thresholds determined by the



regulator. The final ceiling price allowed under the regulations is called the Maximum Rebated Price (MRP).

Pharmacoeconomic analysis is used in Canada and other countries to inform reimbursement negotiations. But it is unsuitable for use in regulation because it is based on data, metrics, and methods for which there are no agreed standards and which at best produce subjective, assumption-dependent estimations. There are well-known conceptual and technical problems and limitations associated with pharmacoeconomic analysis.^{15 16 17} The new guidelines have not resolved these problems.

For example, the PEP is derived from the drug's cost per QALY, which the guidelines refer to as the PVT, but is known elsewhere as the cost-effectiveness (CE) threshold. There is no international standard or consensus regarding the appropriate CE threshold. A 2018 study reviewed the CE thresholds in 17 countries including 8 of the PMPRB11 [EXHIBIT 7]. CE thresholds ranged from 102% of per capita GDP in Sweden up to 391% of per capita GDP in Belgium. On average CE thresholds were 215% of per capita GDP.¹⁸

Subjectivity is obvious in the evolution of the PVA and PVT thresholds proposed by the PMPRB. Under the regulatory changes that are to go into effect in January 2022, new drugs with prices exceeding 150% GDP per capita (or about \$87,000 in 2020 based on GDP per capita of CAN\$58,000.¹⁹) are subject to the PVA. This is higher than the original PVA threshold proposed by the PMPRB in early draft regulations, which was only 50% of GDP per capita. Under the new

EXHIBIT 7. Cost effectiveness thresholds to GDP per capita ratio, 8 PMPRB11 countries

	CE US\$	GDP US\$	CE/GDP
Belgium	\$180,653	\$46,213	3.91
Norway	\$173,971	\$60,357	2.88
Netherlands	\$132,340	\$50,302	2.63
Japan	\$83,938	\$40,406	2.08
United States	\$100,000	\$56,770	1.76
United Kingdom	\$65,871	\$42,522	1.55
Australia	\$63,096	\$47,351	1.33
Sweden	\$50,173	\$48,975	1.02
Average	\$106,255	\$49,112	2.15

Data: Cameron et al (2018); OECD.

regulations, PVT levels range from 170% to 340% of GDP per capita (\$100,000 per QALY to \$200,000 per QALY). This is up from 60% of GDP per capita originally proposed in earlier drafts.²⁰

Similarly, there is no international consensus regarding the appropriate value of a QALY. QALY is a weighted numerical value which is assigned to various potential health conditions. The values are subjectively determined based on responses from public and expert opinion surveys, using a variety of methods of which there is no standard because each are vulnerable to significant limitations. The simplest method asks respondents to weight the importance of health conditions on a scale from zero (death) to one (perfect health). Other methods ask people to choose between alternatives involving a trade-off between quantity and quality of life; or to weight improving the life expectancy of people with full health, versus improving the health expectancy of people with an illness/disability; or to choose between no treatment, and the risk of a treatment with two possible outcomes, one worse and the other better than no treatment. Such methods are not objectively scientific and are susceptible to ethical problems, knowledge limitations and potential bias.²¹

To get to the final MRP, the Guidelines also impose mandatory additional price reductions for products that generate more than \$50 million in annual sales in Canada. PMPRB refers to these price cuts as the market size adjustment factor.

This feature of the guidelines is tantamount to the regulation of profits, not the regulation of prices, and goes well beyond the boundaries of the PMPRB's mandate. There is no precedent for this in any industry in Canada. The policy is extremely hostile to innovation because it imposes diminishing returns on commercially successful products. It will amplify the disincentives for launching new medicines in Canada.

Net Ceiling Prices

The new Guidelines also require patentees to report price and revenues net of all price adjustments. Prices net of rebates will be used to set the ceilings for new medicines. Previously the regulations applied price controls to the manufacturer's ex-factory list price. Manufacturers negotiated rebates with public drug plans and private insurers below list price. The largest discounts were typically offered to public payers due to their superior bargaining power.

There is no published source of product-level data on final prices because rebates are confidential business information protected by contract and constitutional law. In two separate cases, the Federal and Quebec courts recently affirmed these rebates to be constitutionally protected private information. In both cases, the court struck down provisions in the regulatory amendments requiring patentees to disclose rebated prices. The PMPRB is appealing both cases.^{[22](#) [23](#)}

The RIAS cited price discrimination as a rationale for regulating net price ceilings,

“In Canada and other developed countries, it is common practice for medicine manufacturers to negotiate confidential rebates and discounts off public list prices in exchange for having their products reimbursed by public and private insurers. This empowers manufacturers to price-discriminate between buyers based on their perceived countervailing power and ability to pay.”^{[24](#)}

The statement reveals that the PMPRB thinks part of its mandate is to ensure private insurance companies do not pay higher prices for patented medicines than public drug plans pay. However, its actual mandate is to set ceiling prices not final prices. Imposing a single market price would be a mistake. Price differentiation is an economically efficient way to achieve socially equitable outcomes.^{[25](#) [26](#) [27](#)}

At the international level, drug prices tend to be higher in wealthier countries and lower in less wealthy countries. Pharmaceutical companies use price discrimination (or differentiation) to maximize profits across markets with different average incomes. However, the higher prices charged in wealthier countries subsidize lower prices in less wealthy countries, making it possible for consumers to access more medicines that they would otherwise be able to afford.

Price discrimination between payers *within* a market also produces socially equitable outcomes. In Canada, the ability to charge different prices to public and private payers has contributed to more equitable outcomes than would have occurred under a single market price.

The Pan-Canadian Pharmaceutical Alliance (PCPA) conducts joint price negotiations with pharmaceutical manufacturers on behalf of all Provincial and

Territorial public drug plans and cancer care agencies, plus the Federal Non-Insured Health Benefits, Correctional Services of Canada and Veterans Affairs Canada. The PCPA leverages monopsony bargaining power to achieve uniform pricing and reimbursement conditions for public payers. Public drug plans pay prices that are much lower than the manufacturers list price. Ontario's Auditor General reported that the province's public drug plan received rebates averaging 36% on brand name drugs in the fiscal year 2016/17.²⁸

Public sector discounts are made possible because pharmaceutical companies can charge higher prices to private sector payers like insurance companies. While private payers are free to negotiate rebates with manufacturers, there is little evidence that they obtain rebates as large as those reported for public payers. However, private drug plans cover economically secure populations, whereas public drug plans serve economically vulnerable populations. The higher prices charged to private payers subsidize the lower prices negotiated with public payers.

Price discrimination therefore makes it possible for public payers to cover more drugs for more vulnerable people than they would otherwise be able to afford within tax-funded budget constraints. It achieves this without reducing utilization among privately insured populations, who are early adopters of new drugs and thereby fund future innovation.

Differential pricing has likely increased the availability of new drugs in Canada. The potential to obtain higher prices in the private market encourages pharmaceutical manufacturers to launch new drug products in Canada earlier than would otherwise occur with uniform prices set at public market levels.

The fact that public payers have more bargaining power than private payers does not justify the regulations. Private insurers have significant bargaining power relative to pharmaceutical manufacturers. High-cost drugs can cause affordability challenges within some individual drug plans, but this occurs mainly because of insufficient risk pooling. Many employer-sponsored drug plans essentially self-insure their employee population, utilizing the insurer merely for administrative services only. Industry-wide risk pooling is a solution. Government could make it mandatory for all employer-sponsored drug plans to participate. This approach would be more legitimate than using the PMPRB as a cost manager for private sector drug plans.

Regulatory Impact on Prices

According to the Regulatory Impact Analysis Statement (RIAS) published in the regulations, the combined effect of replacing the PMPRB7 with the PMPRB11, introducing PVA, and applying the price controls to net prices, will reduce the maximum allowable prices for high-cost medicines by 52%.²⁹ The impact is likely to be much larger.

The RIAS indicated that changing the reference countries will reduce the *revenues* of high-priority medicines by 4.5%. In a separate analysis, the regulator estimated that, if the new PMPRB11 were implemented in 2019, the MIP would have been 19% lower than Canadian prices.³⁰ Contrast this with the data from my study of the top 100 selling patented medicines, which showed the MIP could range from 10% higher to 5% lower than Canada depending on whether prices were denominated at MER or PPP. Estimates of the MIP are also sensitive to other methodological differences identified later in Chapter 5, making it difficult to estimate the price impact with certainty.

In addition, the regulatory impact analysis estimated that the application of the three new PVA factors (therapeutic criteria, PVT, profit controls) is expected to further lower the price of new high-priority medicines by more than 40% on average. However, the regulations specify mandatory price cuts up to 50% from applying the therapeutic criteria and PVT, and another 35% from profit controls.

The RIAS also estimated that applying price ceilings to the net price would result in a further 7.68% reduction in projected patented medicine costs. The estimate assumed that rebated prices were 10% lower than the list prices reported to the PMPRB. Yet, public payers routinely receive rebates that are four times as large. If the regulations apply price controls to net prices, it will extend public sector rebates to private sector payers and amplify the estimated impact on prices.

Expectations of a deeper impact from the regulations are also supported by results from two independent studies which examined the Guidelines and retrospectively applied them to the case of a recently launched medication for a rare disorder. The researchers found that the Guidelines would have imposed price ceilings from 61% to 84% lower than the actual maximum allowed for those drugs.^{31 32}

Chapter 3: Price and new drug launches

How will extreme price cuts impact industry decisions on whether to launch a new medicine in Canada? The lower price limits could cause pharmaceutical companies to deprioritize the Canadian market when launching new medicines.

PMPRB has ignored any evidence that contradicts its narrative justification for the amendments to the regulations. In the regulatory impact analysis, the Board stated that “prices do not appear to be an important determinant of medicine launch sequencing.”³³

Is there any evidence that new drug launches are affected by company expectations regarding regulated price ceilings? The bulk of research on the subject strongly indicates the answer is yes.

The PMPRB was made aware of a substantial body of research confirming that price was empirically linked to the number of new drug launches, which was referenced by several submissions to the public consultations for the proposed regulatory changes.

I represented Canadian Health Policy Institute's contribution to the public consultations. Some of the evidence cited in my submission included a study by Danzon et al (2004) from the University of Pennsylvania, which analyzed the effect of price regulation on delays in launch of new drugs in 25 major markets, including 85 new chemical entities (NCEs) launched between 1994 and 1998. The study found that countries with lower expected prices had fewer launches and longer launch delays, controlling for per capita income and other country and firm characteristics.³⁴

I also referenced a study by Kyle (2007) which found that price controls had a statistically and quantitatively important effect on the extent and timing of the launch of new drugs, with companies being less likely to introduce products in price-controlled markets.³⁵

In another study, Danzon and Furukawa (2008) compared pharmaceutical spending, availability, use, and prices in twelve countries including Canada in

2005. The researchers found that, based on the full universe of drugs launched in 1995 to 2005 in these markets, countries where drugs can be launched without first requiring government approval of the price, had the shortest average launch lag and the highest percentage of new drugs available.³⁶

The evidence includes research by Costa-i-Font et al (2011) who used a multi-variable regression analysis to examine the delay for drug product launches in 20 major pharmaceutical markets for new molecules from 14 different therapeutic classes. Controlling for other factors, the researchers found a correlation between prices and delayed launches. The findings suggest that delay is longer in lower-priced markets.^{37 38}

PMPRB was also informed about a study by Golec and Vernon (2010) which examined 19 years of data and estimated that price controls in the EU resulted in fewer new drug launches relative to the US.³⁹

The agency knew that Kanavos et al (2019) published a study in the European Journal of Health Economics which showed that manufacturers adopt launch sequencing strategies to mitigate downward price spiral, delaying the launch of new products in low-price countries or in countries with highly regulated prices. Within the EU, this has led to reduced availability of medicines in countries with small markets and lower prices.⁴⁰

The PMPRB should by now be aware of research conducted by Canadians, including a study by Spicer and Grootendorst (2020) which examined drug launches and patented drug list prices for various OECD countries specifically to inform the impact of the PMPRB regulatory changes on drug launch delays in Canada. Regression analysis found that patented drug list prices exert an economically important effect on launch decisions, holding other factors constant. The researchers further estimated that a 25% price decrease in prices would lead to a 6-10% decrease in drugs launched, and a 45% price decrease will lead to a 13-22% decrease in drugs launched.⁴¹

Another recent Canadian study by Rawson (2020) investigated whether the pending introduction of the new regulations and guidelines was associated with early signs of changes in the number of new drugs being launched in Canada. The study found that the percentage of new drugs approved in Canada decreased substantially in the years following the initiation of the legislative

process for the new regulations. The results suggest that the pharmaceutical industry has started to deprioritize drug launches in Canada.⁴²

To be clear, company decisions about where and when to launch a new drug product are a function of several external variables including the size of the market, standards of clinical practice in the therapeutic area, intellectual property rights protection, the presence of competing products, etc. Internal factors also influence the geographic location of drug launches like for example, whether the company has an established local workforce to support the launch. Price is one of many factors companies consider, but it is perhaps the most important variable determining company prioritization of the market launch sequencing for new drugs.

The importance of price was confirmed in a study I conducted in 2018 which tested the statistical relationship between the number of new drug launches and the market price level for patented drugs, GDP per capita and the total market size (population) in each country.⁴³

Data for new drug launches were obtained from the PMPRB.⁴⁴ New drug launches were defined by the PMPRB according to each country's percentage share of the 210 new active substances (NASs) that were launched between 2009 and 2014 in Canada and the PMPRB7. The foreign-to-Canada price ratios for patented drugs in the 31 OECD countries were as reported by the PMPRB.⁴⁵ GDP and population data were obtained from OECD. GDP per capita was current to 2015 denominated in US \$ PPP, and population was current to the most recent common data year available when the analysis was conducted.⁴⁶

EXHIBIT 8 is a scatter plot showing the positive correlation between market price level and new drug launches across the OECD countries. **EXHIBIT 9** shows the results of the regression analysis. Market price level was the only one of the three independent variables that was a statistically significant predictor of the number of new drug launches ($P < .05$, at 95% *CI*). Lower priced markets experienced fewer new drug launches, and vice versa, higher priced markets tended to experience more new drug launches.

EXHIBIT 8. Price and new drug launches in 31 OECD countries

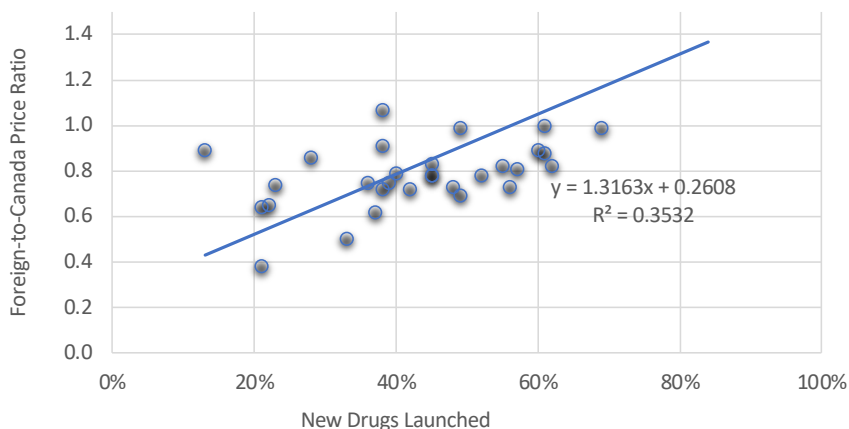


EXHIBIT 9. Price and new drug launches in 31 OECD countries

Dependent variable: New drug launches

Regression Statistics

Multiple R	0.601
R Square	0.361
Adjusted R Square	0.290
Standard Error	0.134
Observations	31

ANOVA

	df	SS	MS	F	Sig F
Regression	3	0.272	0.091	5.093	0.006
Residual	27	0.481	0.018		
Total	30	0.754			

Independent Variables	Coefficients	Standard Error	t Stat	P-value
Intercept	0.181	0.088	2.050	0.050
PRICE	0.283	0.129	2.186	0.038
GDP	0.000	0.000	0.430	0.671
POP	0.000	0.001	-0.216	0.831

Chapter 4: Price and industry-funded pharmaceutical R&D

What will be the effect on industry-funded investment in pharmaceutical research and development? PMPRB has dismissed the concerns of stakeholders that the regulatory changes will discourage pharmaceutical industry funding for clinical trials research in Canada. The agency claims there is no evidence linking price and pharmaceutical R&D. In its regulatory impact analysis, the PMPRB stated:

"It is not anticipated that these amendments would generate adverse impacts on industry employment or investment in the Canadian economy. Although when the current regulatory framework was first conceived 30 years ago, policy makers believed that patent protection and price were key drivers of medicine research and development (R&D) investment, there is no evidence of this link. The level of industry R&D investment relative to sales by medicine patentees in Canada has been falling since the late 1990s and is now at a historic low despite Canada having among the highest patented medicine prices in the world. These amendments would aim to align Canadian prices with those in countries that, despite having lower prices, receive higher medicine industry investment."⁴⁷ "The link between high domestic prices and industry investment has not been demonstrated."⁴⁸

Again, PMPRB must be aware of published research showing a statistical link between price and industry investment in clinical trials because it was referenced as part of several submissions to the public consultations for the proposed regulatory amendments. Yet, the agency has not referenced this empirical evidence in official communications with Parliament. Instead, it cited a single anecdotal reference to justify its position.

Evidence includes a study by Giacotto et al (2005) which analyzed US and European data on price regulation and R&D spending in the pharmaceutical industry. The researchers concluded that regulating pharmaceutical price increases to the rate of inflation from 1980 to 2001, would have decreased R&D spending in the US by 30%.⁴⁹

Other research by Koenig and MacGarvie (2011) examined price regulation and location of biopharmaceutical Foreign Direct Investment (FDI) in Europe. FDI was found to be less likely in countries with price controls. Importantly, because it parallels the pending changes in Canada, researchers found a decline in non-manufacturing investment in countries that increased the stringency of regulatory regimes during the period of study.⁵⁰

In fact, research has already been conducted on changes in the investment behaviour of the pharmaceutical industry following the announcement of the amended regulations. In a series of papers, Rawson (2020-2021) investigated whether there were early warning signs of a decline in clinical trials activity in Canada associated with the publishing of the new price control guidelines in November 2019. The study observed the number of new clinical trials registered before and after the 2019 date. Results showed a significant decrease in trials in Canada following the announcement of the regulatory changes.^{51 52 53} The PMPRB's only response to these empirical studies was communicated via Twitter.

Drilling down into the data reveals a strong positive correlation between price and location of industry investment in pharmaceutical R&D. In a 2019 empirical study, I examined 31 OECD countries for statistical correlations between the geographic distribution of industry-funded clinical trials and variation in drug price levels, controlling for differences in GDP and market size.⁵⁴

Data were available from the PMPRB that compared average ex-factory list prices in 2017 for patented drugs across 31 OECD countries in bi-lateral ratios of foreign-to-Canadian prices denominated in US dollars at purchasing power parity.⁵⁵

Data on the number of industry-funded clinical trials in the 31 OECD countries were obtained from the ClinicalTrials.gov database operated by the U.S. National Institutes of Health.⁵⁶ The data included all industry-funded clinical trials with a registered start date in 2017.

Corresponding 2017 data on GDP per capita and total national population in each of the 31 countries were obtained from the OECD online database.⁵⁷

A statistical analysis was conducted to test for correlations between variation across countries in the number of industry-funded clinical trials (IND CTs) and

differences in prices (F:C IPRX\$), economies (GDP percap) and market size (POP '000s).

EXHIBIT 10 illustrates the positive statistical relationship between price and the geographic distribution of industry-funded clinical trials.

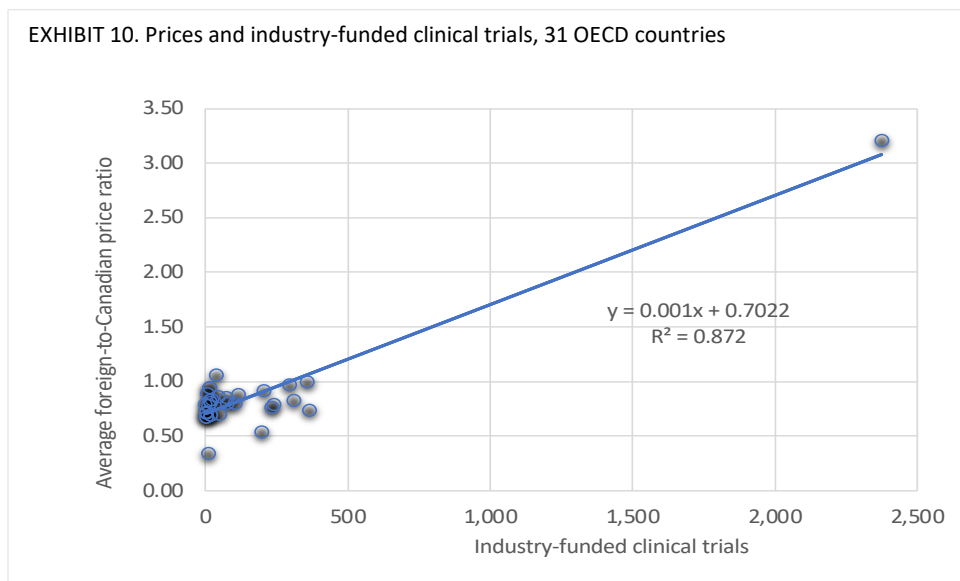


EXHIBIT 11 displays the results of a multi-variable regression analysis to test the statistical significance of price, controlling for the other independent variables in the model. Statistically significant results are highlighted.

Together, the independent variables in the model were a statistically significant (Sig. F = 0.000) predictor of the dependent variable, explaining almost 90% (Adj.RSq.= 0.897) of the variation in the number of industry-funded clinical trials between countries.

The analysis of the correlations between the dependent variable and each independent variable, showed that only price ($P = 0.000$) and market size ($P = 0.004$) remained statistically significant predictors of the dependent variable after controlling for the other independent variables in the model.

The coefficient results show that a 1-unit variation (± 1.00) in the average foreign-to-Canadian price ratio for patented medicines is associated with a variation of ± 613.355 industry-funded clinical trials. This implies that, if the

EXHIBIT 11. Prices and industry-funded clinical trials, 31 OECD countries

Dependent variable: Number of industry-funded clinical trials

Regression Statistics

Multiple R	0.953
R Square	0.907
Adjusted R Square	0.897
Standard Error	136.551
Observations	31

ANOVA

	df	SS	MS	F	Sig F
Regression	3	4929415.634	1643138.545	88.121	0.000
Residual	27	503449.720	18646.286		
Total	30	5432865.355			

Independent Variables	Coefficients	Standard Error	t Stat	P-value
Intercept	-498.919	79.124	-6.306	0.000
PRICE	613.355	101.934	6.017	0.000
GDP	0.001	0.002	0.576	0.570
POP	0.002	0.001	3.141	0.004

average Canadian price had been 50% lower during the years leading up to 2017, Canada would have registered 307 fewer clinical trials in 2017. At current prices Canada had only 357 industry-funded clinical trials with a registered start date in 2017. If the PMPRB had implemented its regulatory agenda in the years prior to 2017 and produced the size of the price cuts predicted, it could have nearly eliminated pharmaceutical research in Canada by 2017.

The results suggest that a lower price ceiling resulting from the PMPRB regulatory changes will likely cause a substantial decline in the number of industry-funded clinical trials in Canada.

Analysis of other data shows that pharmaceutical R&D spending in Canada is declining over time in parallel with a simultaneous decline in the Canadian price level for patented medicines relative to the average of the PMPRB7 reference countries. I examined 11 years of data from PMPRB's annual reports and confirmed that Canadian list prices for patented medicines have been declining relative to the average of the PMPRB7 countries.

The PMPRB publishes foreign prices in ratio to Canadian prices (F:C). **EXHIBIT 12** shows the inverse equivalent Canadian-to-foreign (C:F) ratios. Measured at median prices adjusted for MER, the C:F price ratio fell from 0.97 in 2007 to 0.79

in 2017. Measured at mean prices adjusted for PPP, the C:F price ratio fell from 0.96 in 2007 to 0.65 in 2017.

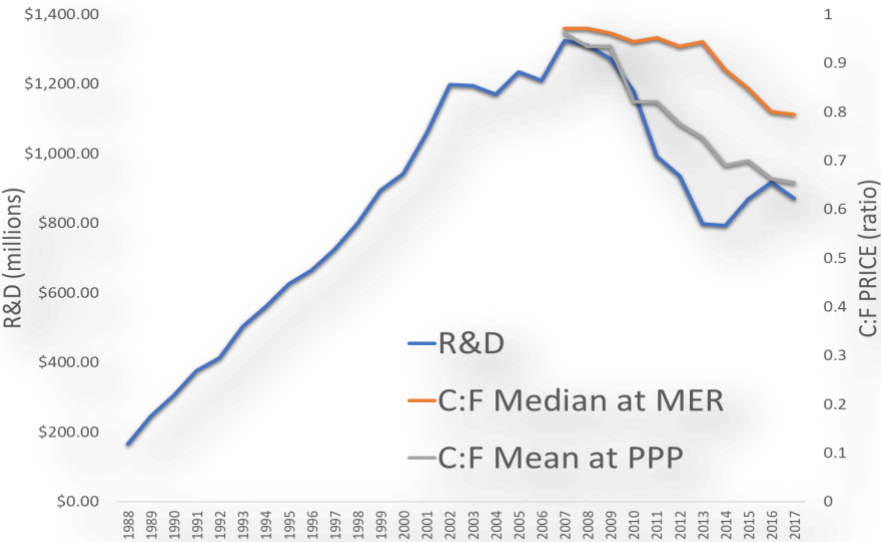
PMPRB data also show that from 2007 to 2017 spending on pharmaceutical R&D in Canada fell from over \$1.325 billion to \$791.1 million.⁵⁸ **EXHIBIT 12** plots R&D spending and C:F price ratios on the same graph using two vertical axes. The decline of spending on R&D coincides with a deteriorating Canadian price level relative to competing markets in the PMPRB7 countries.

It is important to note that there is a statistical lag effect linking industry-funded R&D to the number of clinical trials. Canada accounted for less than 2% (US\$22.2 billion sales) of the global pharmaceuticals (patented and non-patented) market (US\$1,204.8 billion sales) by 2018, yet since 2008 almost 10% (10,080) of the cumulative global total number of industry-funded clinical trials (103,352) have been located in Canada.^{59 60}

The country's relative success attracting industry-funded clinical trials is a legacy from earlier investment decisions when Canada's price level was higher relative to the PMPRB7 comparator countries. A statistical lag between data for R&D spending and the number of clinical trials occurs because clinical trials can take more than 6 years to complete.⁶¹

Declining recent trends in industry investment in pharmaceutical R&D will be reflected in future statistics which should be expected to show a subsequent parallel decline in the number of industry-funded clinical trials located in Canada. The federal government's pending PMPRB regulatory changes will probably exacerbate this trend.

EXHIBIT 12. Canada-to-PMPRB7 price ratio and R&D spending



Data: PMPRB

Chapter 5: Prices for patented medicines

The PMPRB's narrative justification for amending the regulations relies heavily on its claim that Canadian prices are too high relative to other countries as evidenced by Canada's rank in international price comparisons. ⁶² ⁶³ In various publications, the PMPRB has stated, "Canada is paying higher prices for prescription drugs than most other developed countries..." and "Canadian patented drug prices have been steadily rising relative to prices in the seven countries to which Canada compares itself under its regulations..." ⁶⁴ ⁶⁵

The agency relies on its own internal analysis of international drug prices to support this narrative. Despite the potential negative impacts from the implementation of the regulations, the Board's analyses have not been independently audited. Following are some of the limitations associated with the PMPRB price referencing methods, any of which would have a material impact on Canada's rank among PMPRB reference countries.

Exaggerated Significance of International Rankings

International rankings of pharmaceutical prices are not very meaningful because they tend to exaggerate the actual differences between prices. The absolute difference between each rank position is equal to 1.00, which stated as a percentage is equal to 100%. Whereas the difference in prices is often far less than 100%.

List Prices vs Actual Prices

The PMPRB analyzes the cost of drugs at the manufacturer's list price level, which does not reflect actual prices. List prices exclude rebates negotiated between manufacturers and public and private payers. Rebates can vary widely across jurisdictions, and actual prices paid can be substantially lower than the manufacturer's list price used for international comparisons.

Price and Income Variability

International comparisons of nominal price differences do not reflect the actual affordability of patented medicines across countries. OECD countries are used for international comparisons because they have roughly similar developed economies and political systems. However, average incomes vary significantly across OECD countries. For example, 2020 GDP per capita among the 14 countries examined later in this chapter varied from a low of \$38,335 in Spain to a high of \$71,298 in Switzerland, measured in US dollars at purchasing power parity. Research shows that the prices of patented medicines tend to follow variation in average income across countries, other factors held constant.^{66 67 68} Prices tend to be higher in wealthier countries, but account for a lower percentage of average income. Symmetrical comparisons of drug prices should control for income differences between countries. The PMPRB's international price rankings do not account for variation in average income. The results do not reflect the actual cost burden experienced across countries due to patented drug prices.

Case Inclusion Criteria

According to the PMPRB "it is not always possible to find a matching foreign price for every strength and dosage form of a patented medicine sold in Canada... it is not uncommon for the US to be the only comparator country with an available price..."⁶⁹ Yet the PMPRB calculates average foreign-to-Canadian price ratios for patented medicines across the OECD only "for medicines with prices available in at least three foreign markets."⁷⁰ This implies that potential comparisons were excluded from the PMPRB analysis when prices were available in less than three markets. Exclusion of these cases could skew the results.

Basic Unit of Measure

The PMPRB average foreign-to-Canadian price ratios for the OECD countries are reported at the "medicine level".⁷¹ Prices should be compared at the standard unit level which is the number of tablets, millilitres or grams sold, divided by the smallest common dosage. Standard units permit fair comparisons of prices across products with different dosage strengths, pack sizes and sales volumes.

Sales Weights

The average price ratios reported by the PMPRB are “sales-weighted arithmetic means of price ratios obtained for individual DINs, with weights based on Canadian sales patterns.”²² The method produces a hypothetical price. Foreign prices should be weighted by domestic sales volumes which would reflect the actual prices in their domestic market. Using a price per standard unit permits symmetrical comparisons aggregated at the molecule level that are intrinsically weighted by domestic sales volumes.

Domestic Patent Status

It is unclear whether the foreign drug products in the PMPRB’s analysis have the same domestic patent status as the Canadian comparator. A fair comparison of international prices requires equivalent patent protection status in both countries.

Prices in the PMPRB7

The regulator’s own data refutes its alarmist claim about high Canadian prices. The PMPRB 2019 annual report (most recent year) includes bilateral price comparisons with each PMPRB7 country. The data source used for these international price comparisons is the publicly available gross ex-factory manufacturer list prices that patentees are required by regulation to report to the PMPRB.

The 2019 Canadian data sample represented the universe of patented medicines reported to the regulator and was comprised of 1,331 drug products of various dosage strengths and forms accounting for CAN \$17.2 billion in gross sales at manufacturer list prices.

PMPRB also reports the number of foreign drug products matching the Canadian products for each comparator country. The Canadian products paired in the bilateral average price ratios reported for the

EXHIBIT 13. PMPRB7-to Canadian price ratios

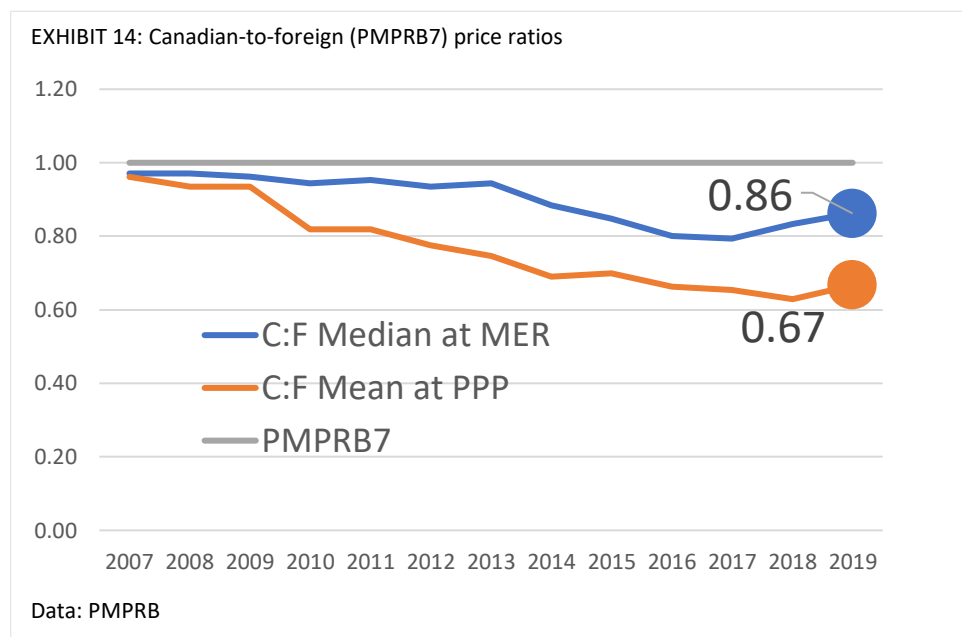
	MER	PPP	DINs
USA	3.77	3.50	1,035
GER	1.07	1.16	980
ITA	0.96	1.15	778
CAN	1.00	1.00	1,331
UK	0.97	0.99	958
SWI	1.04	0.81	858
FRA	0.73	0.79	637
SWE	0.81	0.78	801
PMPRB7	1.34	1.31	864

Data: PMPRB

PMPRB7 represented at least 66% of total Canadian sales in 2019.⁷³ [EXHIBIT 13]

Contrary to the PMPRB's assertion, Canadian prices are not higher than most comparable countries. When prices were denominated in US dollars at market exchange rates (MER), Canada ranked in the middle (fourth) among the PMPRB7 reference countries behind higher-priced countries United States, Switzerland, and Germany. When prices were denominated at purchasing power parity, Canada ranked fourth behind the United States, Germany, and Italy.

Data also contradict the PMPRBs claim that Canadian patented drug prices have been steadily rising relative to the PMPRB7. **EXHIBIT 14** shows Canadian-to-foreign price ratios, holding the foreign average constant. At MER, median Canadian prices were lower than median foreign prices for the last 13 years, as much as 14% lower in 2019. When the PMPRB used mean (or average) prices, and adjusted currencies at PPP, Canadian prices also remained below foreign prices over the entire study period, declining to 33% lower by 2019.



Prices in 14 PMPRB countries

I tested the validity of the PMPRB's narrative about high Canadian prices in a recent study, which I referenced in an earlier chapter.⁷⁴ Recall that the study focused on the patented drugs that would exceed the sales threshold which would make them subject to PVA under the regulation. Specifically, the 100 top selling patented medicines in Canada were compared to prices for symmetrical products in 13 other countries comprised of the PMPRB11 plus former reference countries Switzerland and the United States.

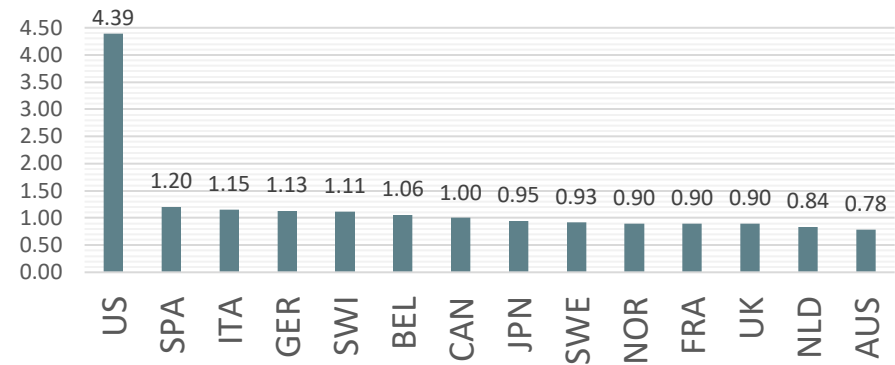
Again, the study used bilateral foreign-to-Canadian price comparisons that were limited to symmetrical drug molecules with the same domestic patent protection status; and the analysis used a standardized unit of measure for calculating foreign-to-Canadian price ratios that is comparable across varied dosage strengths, pack sizes and sales weights: defined as gross sales at manufacturer list prices per standard unit sold.

Average foreign-to-Canadian price ratios were calculated across the ratios observed for each bilateral comparison of molecules. A gap score was also calculated to compare the economic affordability of patented medicines prices relative to income, which was defined as the difference between average foreign-to-Canadian ratios for patented medicines prices and foreign-to-Canadian ratios for GDP per capita. The results are shown below.

EXHIBIT 15 shows that, on average over the three calendar years from 2018 to 2020, Canada ranked seventh of 14 countries when average foreign-to-Canadian price ratios were measured at US dollars MER. The six countries ranking higher than Canada include Belgium (avg 1.06:1), Switzerland (avg 1.11:1), Germany (avg 1.13:1), Italy (avg 1.15:1), Spain (avg 1.20:1), and the United States (avg 4.39:1). Notably, five of the 7 countries ranked below Canada had price ratios within 10% of the Canadian benchmark (Japan, Sweden, Norway, France, and the UK).

International price comparisons that account for differences in average incomes between countries can be used as a comparative measure of economic affordability for the prices of patented medicines. GDP per capita is a proxy for average income. **EXHIBIT 16** shows the gap between average foreign-to-Canadian ratios for patented medicines prices and foreign-to-Canadian ratios for GDP per capita, stated at US dollars PPP and averaged over 2018-2020.

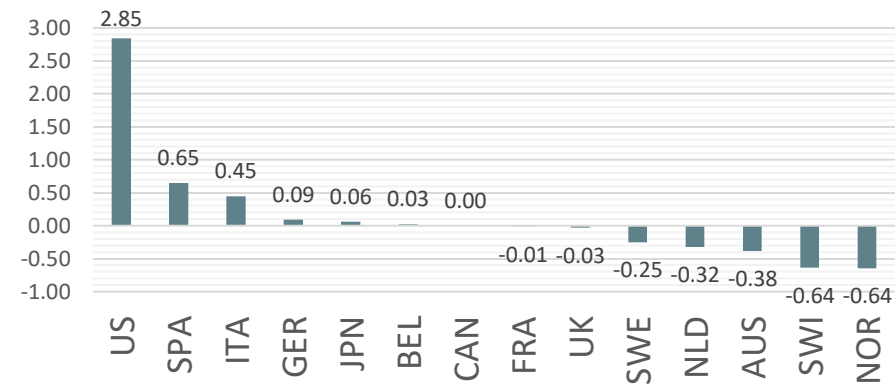
EXHIBIT 15. Foreign-to-Canadian price ratios



Data: IQVIA

The gap was calculated by subtracting the foreign-to-Canadian ratio for GDP per capita from the average foreign-to-Canadian ratio for patented medicines prices. Positive values represent average foreign-to-Canadian price ratios that are greater than corresponding foreign-to-Canadian GDP per capita ratios. Negative values represent average foreign-to-Canadian price ratios that are lesser than corresponding foreign-to-Canadian GDP per capita ratios. Relative to domestic incomes, positive values can be interpreted to mean that on average

EXHIBIT 16. Gap in foreign-to-Canadian ratios for prices and GDP per capita



Data: IQVIA

prices are less economically affordable, while negative values can be interpreted to mean that on average prices are more economically affordable.

On average from 2018 to 2020, Canada ranked seventh of the 14 countries studied in the analysis of foreign-to-Canadian ratios for patented medicine prices and GDP. Two of the seven countries that ranked lower than Canada (France, and the UK) had gap scores within 3 percentage points of Canada's score.

The PMPRB's narrative justification for amending the regulations and guidelines is not supported by the available data. Canada ranked in the middle of the 14 countries studied. There is nothing about Canada's rank that would indicate the prices for patented medicines are excessive. The previous regulations and guidelines are adequate to achieve the government's explicit policy goal and for the PMPRB to fulfil its mandate. The amendments to the regulations and guidelines are not necessary.

Chapter 6: Patented medicines expenditure (PMEX)

Another justification offered by the PMPRB for amending the regulations, is that prices for patented drugs are creating a health care sustainability crisis. In several government documents and discussion papers issued since 2015, the PMPRB has repeated misleading statements including, “Drugs are now the second-largest category of spending in health care...”⁷⁵, and “Since 2000, Canada’s growth in patented drug expenditures as a share of GDP has increased by 184%.”⁷⁶

The regulatory impact analysis presented to parliament stated, “Innovative medicines, including those that are subject to patent protection, help prevent and cure disease as well as save lives. But Canadians are not getting the value for money they deserve relative to total medicine spending, which has increased from 8.5% of the total health care expenditures in 1977 to about 16% today.”⁷⁷ “High-cost” patented drugs were specifically cited as an affordability challenge for public and private payers.”⁷⁸

The statistics cited in the RIAS are based on data from the Canadian Institute for Health information (CIHI) for total drugs and related spending, which is not equivalent to direct spending on patented medicines. CIHI drugs spending statistics cannot be used to justify the Amendments to the Patented Medicines Regulations because the actual costs attributable directly to patented drugs are only a fraction of the total “drugs” costs published by CIHI.⁷⁹

CIHI defines “drugs” expenditure much differently than PMPRB. The data reported by CIHI encompasses total national expenditure at final prices (manufacturer prices, plus wholesale and retail price markups, pharmacy fees and sales taxes) on patented and non-patented (off-patent brands and generics) drugs, prescribed and non-prescribed drugs, personal health supplies, administrative costs of public drug plans, and spending by pharmaceutical companies on drug research. CIHI **excludes** hospital spending on drugs, which is included in “hospital” expenditure.⁸⁰

PMPRB is the only public source of national data for direct spending on patented medicines in Canada. The data for “patented drugs” sales reported by PMPRB **includes** total national sales of prescribed and non-prescribed patented drugs at manufacturer (*ex factory*) gross ‘list’ prices and includes hospital and non-hospital expenditures. PMPRB **excludes** confidential price rebates (discounts) negotiated between manufacturers and public-sector drug plans, private-sector health insurers, wholesalers, retailers, and hospitals.⁸¹

In 2019, CIHI reported \$34.4 billion was spent on “prescribed drugs”, plus \$5.9 billion on “non-prescribed drugs”, for a sum of \$40.3 billion on non-hospital “total drugs” expenditure. CIHI separately reported an additional \$2.5 billion was spent by hospitals on drugs.⁸² The grand total of hospital and non-hospital “drugs” expenditure reported by CIHI amounts to \$42.8 billion in 2019.

According to PMPRB, *gross* national sales of patented drugs were \$17.2 billion in 2019, which accounts for 40% of the “drugs” total reported by CIHI for the same year. Again, this is at manufacturer ‘list’ prices. Final prices actually paid, are net of rebates negotiated between manufacturers and public and private payers. After accounting for these rebates, the share of “drugs” expenditure going to patented medicines would be even smaller.

Contextual analysis of the proper data sources reveals a very different story from the narrative used to justify the amendments. The Canadian Health Policy Institute publishes an annual analysis of patented medicines expenditure relative to national health expenditure, GDP, population, and inflation (consumer price index or CPI).⁸³ The analysis uses the most recent data from the PMPRB, CIHI, and Statistics Canada. Every aggregate measure confirms that spending on patented medicines in Canada is both affordable and sustainable and has been for a long time.

NHEX

One way to measure the affordability and sustainability of expenditure on patented drugs as to compare it to spending on other types of healthcare. At \$17.2 billion, gross national sales of patented drugs accounted for 6.5% of the \$265.5 billion reported by CIHI for national health spending in Canada in 2019 [EXHIBIT 17]. Over the 30 years from 1990 to 2019, spending on patented medicines never exceeded 8.0% of national health expenditure [EXHIBIT 18]. Patented drugs’ percentage of national health spending was almost the same in

2019 as in 2000 (6.4%): a remarkable 20-year period of near zero average annual relative expenditure growth [**EXHIBIT 18**].

High-cost drugs

PMPRB publishes data for national expenditure on high-cost patented drugs (as a sub-category of all patented drugs) covering the period from 2006 to 2019. PMPRB defines high-cost patented drugs as medicines with annual treatment costs of more than \$10,000. According to PMPRB there were 172 patented medicines defined as high-cost drugs in 2019 accounting for \$8.3 billion in gross sales.⁸⁴ Gross sales of all high-cost patented drugs represented only 3.1% of national health expenditures [**EXHIBIT 18**] in 2019.

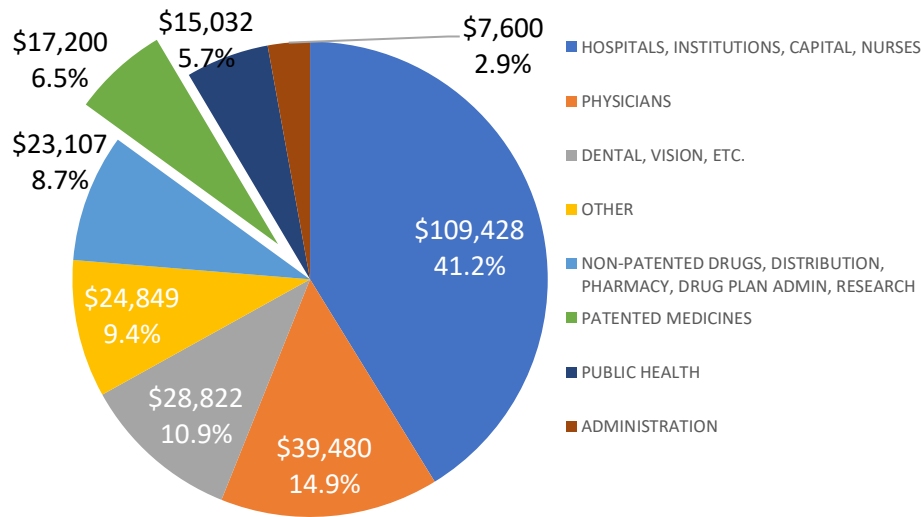
GDP

Gross national sales of patented drugs have accounted for less than 1% of GDP for the last 30 years [**EXHIBIT 19**]. Patented medicines expenditure was approximately the same percentage of GDP in 2019 (0.7%) as in 2003 (0.8%), a 17-year period of zero average annual growth relative to GDP.

Population and inflation

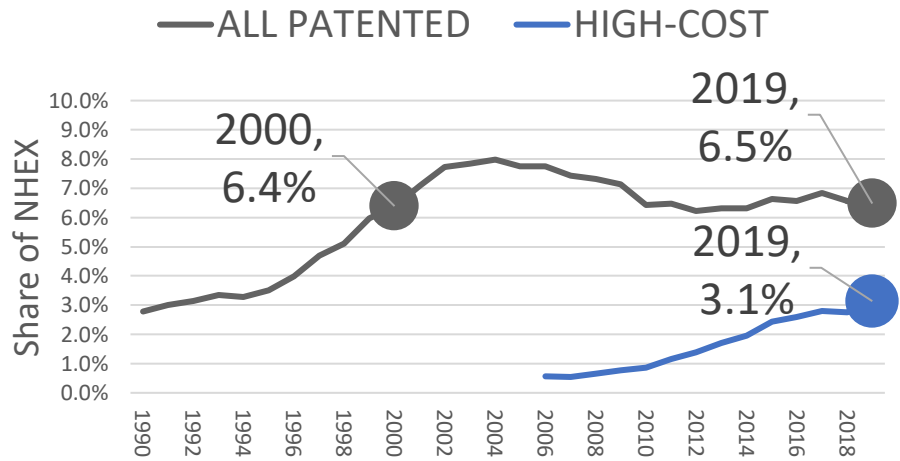
Stated in current dollars, patented medicines expenditure per capita was \$458 in 2019 [**EXHIBIT 20**]. Historical data from 1990 to 2019 were available for population and the CPI that allowed for a conversion of gross national sales of patented medicines into per capita costs stated in constant 1990 dollars to remove the effect of general price inflation. Deflating costs from the beginning of the period (constant 1990 \$) shows the impact of general price inflation over the study period (1990 to 2019) starting from a common point versus the current dollar baseline. Adjusting for national population growth and inflation over time, reveals that national expenditure on patented medicines has experienced zero real average annual growth for the last decade. Stated in constant 1990 dollars, the real gross expenditure per capita on patented drugs was \$264 in 2019 and \$265 in 2009.

EXHIBIT 17: Patented medicines share of national health expenditure C\$ millions



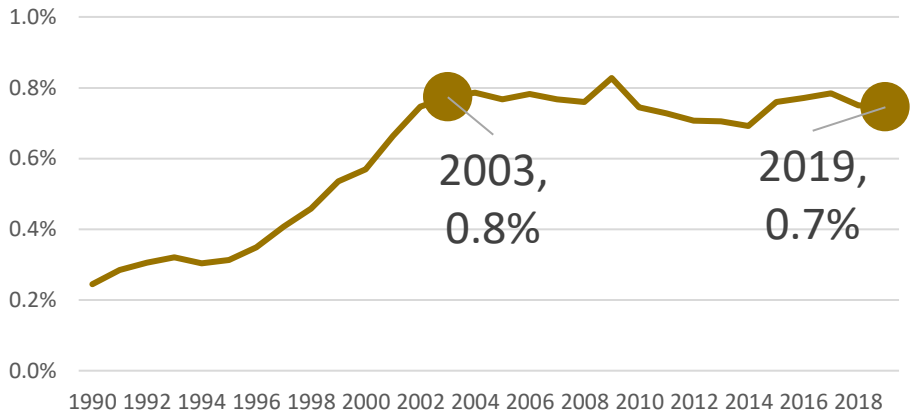
Data: CIHI, PMPRB

EXHIBIT 18: Patented medicines share of national health expenditure



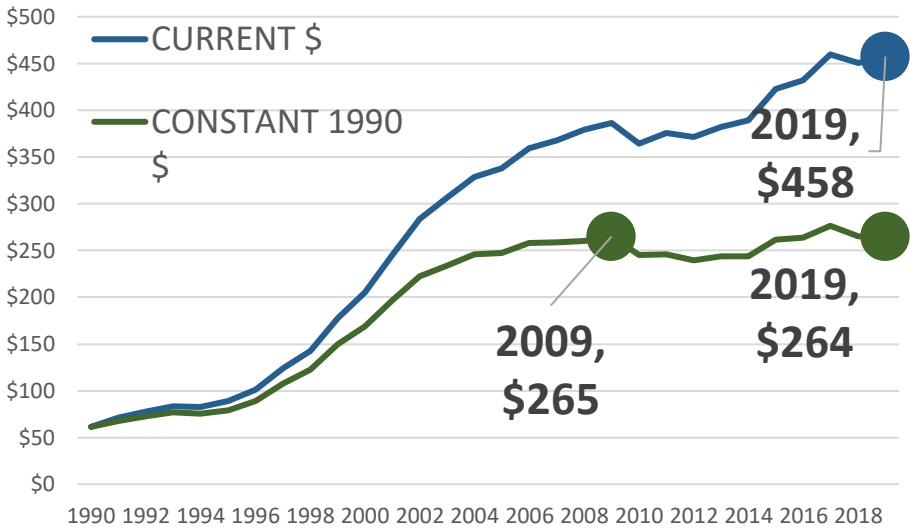
Data: CIHI, PMPRB

EXHIBIT 19: Patented medicines share of GDP



Data: CIHI, PMPRB

EXHIBIT 20: Patented medicines expenditure per capita



Data: CIHI, PMPRB, STATCAN

Chapter 7: Cost v Benefits

Public policy should maximize societal welfare over the long-run.⁸⁵

Governments should consider the net benefits to society from spending more or less on healthcare versus other items in the government budget; and from spending more or less on pharmaceuticals versus other medical and non-medical items within the health budget. Net societal benefits should include the potential costs avoided for healthcare and informal care, plus health-related productivity gains (or losses avoided) that are attributable to the reduction of mortality and morbidity; and the implicit value of future health gains from funding innovation in the current period.

Concerns about the cost of patented drugs must be weighed against the health-economic benefits. Pharmaceutical innovation improves patient health outcomes, reduces potential health system costs, and reduces indirect societal costs like economic productivity losses from untreated or under-treated illness.

There is a huge literature that empirically demonstrates the benefits of pharmaceutical innovation. A systematic review conducted in 2019, found 68 studies published in peer-reviewed academic journals from 1990 to 2018 confirming that greater use of innovative pharmaceuticals is empirically associated with treatment efficiencies and net societal health and economic benefits.⁸⁶

The research literature includes a 2016 study of the impact that pharmaceutical innovation had on utilization of hospital care by cancer patients in Canada from 1995 to 2012. During this period, the number of cancer patient hospital days declined by 23%, even though the number of new cancer cases diagnosed increased by 46%. The study showed that the types of cancer (breast, prostate, lung, etc.) that experienced more innovation in pharmaceutical treatments had larger declines in utilization of hospital care. If no new drugs had been registered during the 1980-1997 period, there would have been 1.72 million additional cancer patient hospital days in 2012, at a cost of \$4.7 billion in hospital expenditure, whereas total spending on cancer drugs (old and new) in 2012 was an estimated \$3.8 billion.⁸⁷

In 2015 another study using Canadian data found that the types of cancer that experienced greater innovation in pharmaceutical treatments had larger

declines in the premature mortality rate, controlling for changes in the incidence rate. The study found that, in the absence of pharmaceutical innovation during the period 1985-1996, the premature cancer mortality rate would have increased about 12% during the period 2000-2011. Most of the innovative drugs were off-patent by 2011, but evidence suggests that, even if these drugs had been sold at branded rather than generic prices, the cost per life-year gained would have been below US\$5,000, a figure well below even the lowest estimates of the value of a life-year gained.⁸⁸

A 2013 study examined the health-economic benefits associated with spending on pharmaceuticals in Ontario from 2007 to 2012. The study found that the added costs associated with the use of innovative pharmaceuticals were offset by reductions in the use of other types of health care resources and a reduction in the productivity losses associated with disease because of improved health outcomes. In particular, the \$1.2 billion spent on six classes of pharmaceutical drugs in 2012 generated offsetting health and societal benefits of nearly \$2.4 billion in the same year.⁸⁹

A 2012 study examined the impact of access to innovative pharmaceuticals on life expectancy using data on 30 countries during the period 2000-2009, finding that life expectancy increased faster in countries using newer drugs. In fact, pharmaceutical innovation explained 73% of the observed increase in life expectancy.⁹⁰

A 2009 study evaluated the impact of access to new medicines on patient survival in a study population of 102,743 subjects using Quebec's provincial health plan data. The study found that the use of newer medications was associated with a statistically significant mortality risk reduction relative to older medications and concluded that drug innovation had a significant beneficial impact on the longevity of elderly patients.⁹¹

A 2005 study found a strong statistical relationship between drug spending and health outcomes, especially for infant mortality and life expectancy at 65. The analysis showed that substantially better health outcomes are observed in provinces where higher drug spending occurs. Simulations showed that if all provinces increased per capita drug spending to the levels observed in the two provinces with the highest spending level, an average of 584 fewer infant deaths per year and over 6 months of increased life expectancy at birth would result.⁹²

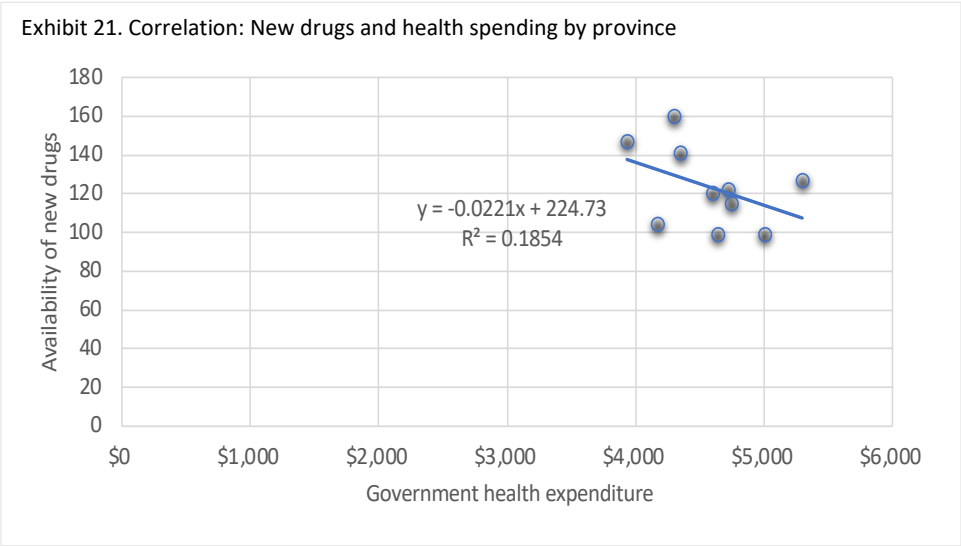
A 2002 study using data on the entire U.S. population from 1996 to 1998 found that the use of newer drugs reduced non-drug spending by 7.2 times as much as drug spending.⁹³

This is just a small sampling of the research on the subject. A few years ago, I compared the availability of medical resources and government health expenditure across the healthcare systems in the ten Canadian provinces to test for any statistical correlations between the variables. I used the most recent comparable data on 5 indicators of the availability of medical resources across provincial health systems, plus 4 indicators for government spending on health care, plus 2 control variables. Specifically, the variables included:

- Practicing physicians (PHYS) per 100,000 population, combined General Practitioners and Specialists.
- Practicing nurses (NURS) per 100,000 population, Registered Nurses (including Nurse Practitioners) employed in profession.
- Acute care hospital beds (HOSPBEDS) per 100,000 population.
- High technology medical diagnostic units (MEDTEC) per 1,000,000 population, combined:
 - Computed Tomography (CT)
 - Magnetic Resonance Imaging (MRI)
 - Position Emission Tomography (PET) - MRI
 - PET-CT
 - Single-Photon Emission Computed Tomography (SPECT)
 - SPECT-CT
- New medicines (NEWDRUGS) covered by public drug plans as of June 30 2018, of the 479 new drugs approved by Health Canada from 2008-2017.
- Provincial government health expenditure (GHEX) per capita.
- Provincial government expenditure on physicians (GPHYSEX) per capita.
- Provincial government expenditure on hospitals (GHOSPEX) per capita; including operating costs and nurses, capital expenditures and other institutions.
- Provincial government expenditure on prescribed drugs (GDRUGEX) per capita; including patented and generic prescribed drugs at manufacturer prices, plus wholesale and retail price markups, pharmacy fees, drug plan administration and other costs.
- Gross domestic product (GDP) per capita.

- Percentage of the population aged 65 years and over (POP%65+).

The most recent available data were current to 2017. Data on physicians, nurses, hospital beds, health expenditure and GDP were obtained from the Canadian Institute for Health Information (CIHI). Data on the number of MRI units, CT, SPECT and PET scanners were obtained from the Canadian Agency for Drugs and Technologies in Health (CADTH). Data related to the public coverage of new medicines were extracted from a report published annually by Canadian Health Policy Institute (CHPI), which used source data from IQVIA. Data on the percentage of the population aged 65 years and over were obtained from Statistics Canada.



Statistical analysis was performed to test for correlations between the medical resources and spending variables. **EXHIBIT 21** is a scatterplot illustrating a negative correlation between the availability of new medicines on the public drug plan formulary and total government health expenditure.

EXHIBIT 22 displays the correlation statistics output in a matrix followed by multi-variable regression analysis to test for statistical significance between correlated variables, where the dependent variable is government health expenditure (GHEX), while all other variables are independent. Negative

numbers indicate an inverse relationship between variables. Statistically significant ($P < 0.05$) results are highlighted.

The analysis of correlations showed that the availability of new medicines on the public formulary (NEWDRUGS) was in an inverse relationship with government health expenditure (GHEX) and with the availability of nurses (NURS) and hospital beds (HOSPBEDS) and in a direct relationship with the availability of physicians (PHYS) and high-tech medical diagnostic devices (MEDTEC).

The set of independent variables in the regression model were a statistically significant ($Sig. F = 0.013$) predictor of the dependent variable, explaining over 98% ($Adj.RSq. = 0.983$) of the variation between provinces for government health expenditure (GHEX).

Regression analysis confirmed that the inverse relationship between NEWDRUGS and GHEX was statistically significant ($P = 0.020$). The regression coefficient ($Coeff. = -20.010$) implies that for every 1 unit increase in the availability of NEWDRUGS between provinces, there was an associated *decrease* in GHEX per capita of \$20.01 net of the variation of all other variables in the model.

The inverse relationship between the availability of NEWDRUGS and resources related to inpatient hospital care (NURS, HOSPBEDS) is expected, due to technological substitution. There is a substantial body of research showing pharmaceutical treatment has made it possible to substitute outpatient treatment for hospitalization, and has reduced lengths of stay in hospital, reduced return visits to hospital and produced better overall health outcomes resulting in lower potential health expenditures than would have been expected in the absence of access to pharmaceutical innovation.⁹⁴

Exhibit 22. Regression Test: New drugs and health spending by province

Dependent Variable: GHEx

Correlations

	GHEx	PHYS	NURS	HOSPBEDS	MEDTEC	NEWDRUGS	GDP	POP%65+
GHEx	1.000							
PHYS	0.092	1.000						
NURS	0.666	-0.055	1.000					
HOSPBEDS	0.658	0.172	0.928	1.000				
MEDTEC	0.370	0.703	0.500	0.632	1.000			
NEWDRUGS	-0.431	0.262	-0.115	-0.073	0.528	1.000		
GDP	0.366	0.118	-0.343	-0.270	-0.138	-0.284	1.000	
POP%65+	-0.172	0.216	0.508	0.514	0.486	0.330	-0.814	1.000

Model

Regression Statistics

Multiple R	0.998
R Square	0.996
Adjusted R Square	0.983
Standard Error	52.919
Observations	10

ANOVA

	df	SS	MS	F	Significance F
Regression	7	1459241.151	208463.022	74.440	0.013
Residual	2	5600.849	2800.424		
Total	9	1464842.000			

Independent Variables

	Coefficients	Standard Error	t Stat	P-value
Intercept	7789.163	999.525	7.793	0.016
PHYS	-12.376	2.984	-4.147	0.054
NURS	0.353	0.597	0.592	0.614
HOSPBEDS	-1.758	0.915	-1.922	0.195
MEDTEC	77.743	12.557	6.191	0.025
NEWDRUGS	-20.010	2.901	-6.899	0.020
GDP	0.001	0.004	0.207	0.855
POP%65+	-6637.257	1662.319	-3.993	0.057

Chapter 8: Rogue Regulator

False Narrative, Risky Regulation

The PMPRB has presented a false narrative about patented medicine prices, while advocating for the expansion of its regulatory powers. None of the PMPRB's alarmist claims stand up to objective scrutiny.

The Board has not provided any credible evidence that the prices of patented medicines are a major driver of national health expenditure. Patented medicines are a small fraction of national health expenditure, even at manufacturer 'list' prices. Net of rebates negotiated between manufacturers and public, and private payers, expenditure on patented medicines would be even smaller. National expenditures on patented medicines are affordable and sustainable. Adjusting for factors like population, CPI and GDP, expenditure on patented medicines has been stable or declining for more than a decade.

The regulator has exaggerated the difference between Canadian prices for patented medicines and prices in other countries. Canadian prices for patented medicines have consistently remained in the middle or below the average of the current (PMPRB11) and former (PMPRB7) countries referenced by the PMPRB.

The PMPRB has failed to keep Parliament informed of research that counters its narrative. There is no excuse for this. It dismissed the concerns of stakeholders as lacking evidence, when in fact the overwhelming weight of published research strongly suggests that the new price regulations are extreme and will delay the launch of new drugs in Canada and discourage industry investment in clinical pharmaceutical research in this country.

The agency is aware of this research because it was cited by several independent submissions to the public consultations held prior to the adoption of the regulations and guidelines. It is not sufficient for the Board to summarize feedback from the public consultations as it did in the regulatory impact analysis that was part of the amended regulations. Merely reporting who said what during the consultation is no substitute for an actual review of published evidence. It's not OK for the regulator to report anecdotes and cite irrelevant statistics, while suppressing scientifically rigorous analyses because they undermine the official narrative.

Public Accountability and the Duty of Neutrality

The PMPRB has also demonstrated a pattern of behavior that reveals a blatant disregard for public accountability and the public service duty of neutrality.

The judicial system has taken note of the agency's rogue behaviour. On July 29, 2021 the Federal Court of Appeal ruled against the PMPRB in a case involving the pharmaceutical company Alexion and its drug SOLIRIS. In an unprecedented decision, the Board deemed the price for Soliris to be excessive, by applying a new price test based on the lowest international price comparison (LIPC), which required the drug to be priced lower than any PMPRB reference country. The Court of Appeal stated that under the Patent Act, the jurisdiction of the PMPRB is limited to preventing the abuse of the monopoly pricing power associated with a patent. It judged that the Board went beyond its statutory mandate, engaging in the regulation of what it viewed to be "reasonable" prices for medicines, rather than its proper mandate, which is to determine whether a medicine's price is "excessive". The Court did not accept that the PMPRB had a consumer protection mandate and concluded that the Board's actions were "constitutionally suspect" and its hostile, uncooperative administrative style lacked transparency and prevented appropriate review of its regulatory decisions.⁹⁵

The PMPRB has not maintained public service neutrality, and its independence has allowed it to avoid political accountability. The agency carried out a public relations and media campaign designed to discredit citizen stakeholders that are opposed to the amendments. In a 2021 document outlining its communications plan, the agency accused opponents of "spreading disinformation" and "knowingly disseminating false information" about proposed changes to the regulations and guidelines. The document detailed plans to use traditional and social media, speaking opportunities and publications to advocate for the regulator's policy agenda and delegitimize opposition.⁹⁶

The Globe and Mail reported on the lack of neutrality at the agency with one columnist writing,

"When officials at the Patented Medicine Prices Review Board were brainstorming a while back about how to sell the Trudeau government's proposed new drug-price regulations, they could hardly contain their

contempt for the pharmaceutical companies they counted as adversaries.

"Industry has been sucking Canada for decades," Tanya Potashnik, the PMPRB's director of policy and economic analysis, wrote in a late 2019 e-mail to colleagues recently obtained through an Access to Information request by Conservative MP Tom Kmiec.

The e-mail chain and other PMPRB documents posted to social media in recent days by Mr. Kmiec portray a regulatory agency that appears bent on sticking it to Big Pharma and obsessed with discrediting the board's perceived adversaries, including some patient advocates.

One such advocate was so incensed by what he saw that he wrote last week to MPs on the House of Commons health committee studying the drug-price proposals to express his indignation: "The PMPRB is a quasi-judicial body that needs to be impartial and objective," wrote Chris MacLeod, chair of the Canadian Cystic Fibrosis Treatment Society. "It is not the voice to be challenging patient groups. Its role is to administer regulations that are developed and promulgated by government, not to undertake lobbying and advocacy strategies."⁹⁷

It is highly unusual and very inappropriate for public servants to display such a lack of neutrality. The rogue behaviour of the PMPRB has been criticized by other patient advocacy groups including the Canadian Organization for Rare Disorders (CORD).⁹⁸ At CORD's request, renowned Canadian professor of political science at the University of Moncton, Donald J. Savoie analyzed the behaviour of the PMPRB and its advocacy plan.⁹⁹ According to Savoie,

"PMPRB's communications plan raises questions about respecting the "Duty of Neutrality" expected of quasi-judicial bodies. I am attaching a PMPRB communications plan to make the point. The plan hardly paints a picture of a quasi-judicial agency that values a sense of detachment and a desire to go about its work free of any bias. I encourage the reader to have a careful read of the plan. Among other points, the plan argues that: the industry puts profits first and patients a distant second; they are knowingly disseminating false information; the industry is holding Canadians for ransom; the need to target supporters of the reform;

identify stakeholders who are not fully supportive of the PMPRB and the list goes on.”¹⁰⁰

Conclusion

The PMPRB has not maintained policy neutrality. The agency is in an obvious conflict of interest: It publicly advocates for amendments which it authored, in a process it initiated and manages, with no accountability or oversight by elected officials. The agency has not presented parliament with a comprehensive, balanced, objective, uncensored summary of all available evidence, for and against the amendments. The agency has suppressed evidence that contradicts its narrative justification for amending the regulations and guidelines. It has dismissed serious concerns about the impact of the regulations on the availability of medicines and industry investment in clinical research without any reference to evidence.

The potential unintended consequences from the new pricing rules are significant. The regulations will delay the availability of new medicines for Canadian patients, causing the loss of the associated health and economic benefits. The new rules will also disincentivize investment in clinical research. Canada's medical science infrastructure may suffer the permanent loss of valuable technical expertise and institutional knowledge.

The federal government is obligated to reconcile the PMPRB's narrative with the evidence presented in this book. The Parliament of Canada should conduct a formal review of the agency's relevance. Due consideration should be given to retiring its mandate.

About the Author



Brett J Skinner (Ph.D., M.A., B.A.)

Brett J Skinner is the Founder and CEO of Canadian Health Policy Institute (CHPI) and the Editor of CHPI's online journal Canadian Health Policy. Dr. Skinner was Executive Director Health and Economic Policy at Innovative Medicines Canada (2013 to 2017); and CEO (2010 to 2012) and Director of Health Policy Studies (2004 to 2012) at Fraser Institute. Dr. Skinner has B.A. and M.A. degrees from the University of Windsor with joint studies at Wayne State University, and a Ph.D.

from Western University where he has lectured in both the Faculty of Health Sciences and the Department of Political Science. In 2015 Brett was diagnosed with early onset Parkinson's disease. He has both an academic interest and a personal health stake in government choices affecting future medical innovation.

References

- 1** Alston, Richard & Kearl, J & Vaughan, Michael. (1992). Is There a Consensus Among Economists in the 1990s? *American Economic Review*. 82. 203-09.
- 2** Daniel P. Kessler (2004). The Effects of Pharmaceutical Price Controls on the Cost and Quality of Medical Care: A Review of the Empirical Literature. Stanford University, Hoover Institution, and the National Bureau of Economic Research.
- 3** Robert B. Helms (2004). The economics of price regulation and innovation. *Managed Care*. 2004 Jun; 13(6 Suppl): 10-2; discussion 12-3, 41-2.
- 4** Canadian Health Policy Institute (CHPI). Evidence that innovative medicines improve health and economic outcomes: focused literature review. *Canadian Health Policy*, April 2019. https://www.canadianhealthpolicy.com/product_articles/evidence-that-innovative-medicines-improve-health-and-economic-outcomes--focused-literature-review-.html
- 5** Douglas Clark (Mar 19, 2020). Counterpoint: Low prices won't keep new medicines out of Canada: *There is no evidence of a link between pricing, research and development, and access to medicine, says Douglas Clark*. *Financial Post*. <https://financialpost.com/opinion/counterpoint-low-prices-wont-keep-new-medicines-out-of-canada>
- 6** Regulations Amending the Patented Medicines Regulations (Additional Factors and Information Reporting Requirements): SOR/2019-298. *Canada Gazette*, Part II, Volume 153, Number 17. Registration: SOR/2019-298, August 8, 2019. PATENT ACT: P.C. 2019-1197 August 7, 2019.
- 7** PMPRB (2021). PMPRB Guidelines. <https://www.canada.ca/content/dam/pmprb-cepmb/documents/legislation/guidelines/PMPRB-Guidelines-en.pdf>
- 8** Health Canada (2017). Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations. Page 3. Abbreviated.
- 9** Regulations Amending the Patented Medicines Regulations (2019).
- 10** Regulations Amending the Patented Medicines Regulations (2019). Page 5992.
- 11** Labrie, Yanick (2020). Evidence that regulating pharmaceutical prices negatively affects R&D and access to new medicines. *Canadian Health Policy*, June 2020. <https://www.canadianhealthpolicy.com/products/evidence-that-regulating-pharmaceutical-prices-negatively-affects-r-d-and-access-to-new-medicines-.html>
- 12** PMPRB (2017). *Meds Entry Watch*, 2015. Figure A1.5 Comparison of the number of NASs available in Canada with those launched in PMPRB7, Q4-2015. Ottawa: Patented Medicine Prices Review Board.

- 13** PMPRB (2020). Annual Report 2019. Figure 24.
- 14** Skinner, Brett (2021). Prices for Patented Medicines in Canada and 13 Other Countries: Testing the PMPRB's Narrative Justification for Amending the Regulations. *Canadian Health Policy*, August 2021. www.canadianhealthpolicy.com
- 15** George A. Diamond, Sanjay Kaul (2009). Cost, Effectiveness, and Cost-Effectiveness. *Circ Cardiovasc Qual Outcomes*. 2009;2:49-54.
- 16** Hill SR, Mitchell AS, Henry DA. Problems with the interpretation of pharmacoeconomic analyses: a review of submissions to the Australian Pharmaceutical Benefits Scheme. *JAMA*. 2000 Apr 26;283(16):2116–21. doi: <http://dx.doi.org/10.1001/jama.283.16.2116> PMID: 10791503
- 17** Pettitt D, Raza S, Naughton B, Roscoe A, Ramakrishnan A, Ali A, Davies B, Dopson S, Hollander G, Smith JA, Brindley DA (2016). The limitations of QALY: a literature review. *J Stem Cell Res Ther* 6: 4.
- 18** David Cameron, Jasper Ubels and Fredrik Norström (2018). On what basis are medical cost-effectiveness thresholds set? Clashing opinions and an absence of data: a systematic review. *GLOBAL HEALTH ACTION*, 2018. VOL. 11, 1447828. <https://doi.org/10.1080/16549716.2018.1447828>.
- 19** CIHI (2021). NHEx Database 1975 to 2021. Canadian Institute for Health Information.
- 20** Canada Gazette Publications Part I: Vol. 151, No. 48 — December 2, 2017. Regulations Amending the Patented Medicines Regulations. REGULATORY IMPACT ANALYSIS STATEMENT. Government of Canada. <http://gazette.gc.ca/rp-pr/p1/2017/2017-12-02/html/reg2-eng.html>.
- 21** Bjarne Robberstad (2005). QALYs vs DALYs vs LYs gained: What are the differences, and what difference do they make for health care priority setting? *Norsk Epidemiologi* 2005; 15 (2): 183-191.
- 22** Innovative Medicines Canada v. Canada (Attorney General). Federal Court Decisions Database. 2020-06-29. 2020 FC 725. T-1465-19
- 23** Merck Canada Inc. et al v Canada (Attorney General), Quebec Superior Court file 500-17-109270-192.
- 24** Regulations Amending the Patented Medicines Regulations (2019). Page 5952-5954.
- 25** Patricia M. Danzon (2018). Differential Pricing of Pharmaceuticals: Theory, Evidence and Emerging Issues. *PharmacoEconomics*. <https://doi.org/10.1007/s40273-018-0696-4>.
- 26** Patricia Danzon, Adrian Towse, Jorge Mestre-Ferrandiz (2015). Value-Based Differential Pricing: Efficient Prices for Drugs in a Global Context. *Health Economics* 24: 294–301 (2015).
- 27** Lichtenberg, Frank R., Pharmaceutical Price Discrimination and Social Welfare. *Capitalism and Society*, Vol. 5, Issue 1, Article 2, 2010. Available at SSRN: <https://ssrn.com/abstract=2208666>.

28 Office of the Auditor General of Ontario. Annual Report 2017. Section 3.09 Ontario Public Drug Programs. Page 491.

29 Regulations Amending the Patented Medicines Regulations (2019).

30 NPDUIS Patented Medicine Prices Review Board February 2021 Meds Entry Watch, 5th Edition.

31 Rawson, Nigel SB; Lawrence, Donna (2020). New Patented Medicine Regulations in Canada: Updated Case Study of a Manufacturer's Decision-Making about a Regulatory Submission for a Rare Disorder Treatment. Canadian Health Policy, January 2020.
<https://www.canadianhealthpolicy.com/products/new-patented-medicine-regulations-in-canada-updated-case-study---en-fr-.html>

32 PDCI (2020). Impact Analysis of The Draft PMPRB Excessive Price Guidelines.
https://www.pdci.ca/wp-content/uploads/2020/02/PDCI-PMPRB-Impact-Assessment-February-2020_Final.pdf

33 Regulations Amending the Patented Medicines Regulations (2019). Page 5992.

34 Patricia M. Danzon, Y. Richard Wang and Liang Wang (2005). The impact of price regulation on the launch delay of new drugs – evidence from twenty-five major markets in the 1990s. Health Economics, 14: 269–292 (2005).

35 Margaret K. Kyle (2007). Pharmaceutical Price Controls and Entry Strategies. Review of Economics and Statistics, Volume 89 | Issue 1 | February 2007 p.88-99.

36 Patricia M. Danzon and Michael F. Furukawa (2008). International Prices And Availability Of Pharmaceuticals In 2005. Health Affairs 27, no. 1 (2008): 221–233; 10.1377/hlthaff.27.1.221.

37 Joan Costa-i-Font, Nebibe Varol, Alistair McGuire (2011). Does price regulation affect the adoption of new pharmaceuticals? The Centre for Economic Policy Research.
<http://voxeu.org/article/does-price-regulation-affect-adoption-new-pharmaceuticals>.

38 Nebibe Varol & Joan Costa-i-Font & Alistair McGuire (2011). Explaining Early Adoption of New Medicines: Regulation, Innovation and Scale. CESifo Working Paper Series 3459, CESifo Group Munich.

39 Golec & Vernon (2010). Financial effects of pharmaceutical price regulation on R&D spending by EU versus US firms. PharmacoEconomics, 28(8), 615–628.

40 Panos Kanavos, Anna-Maria Fontrier, Jennifer Gill, Olina Efthymiadou (2019). Does external reference pricing deliver what it promises? Evidence on its impact at national level. The European Journal of Health Economics.

41 Spicer, Oliver and Paul Grootendorst (2020). An Empirical Examination of the Patented Medicine Prices Review Board Price Control Amendments on Drug Launches in Canada. Working Paper No: 200003. July 2020. Canadian Centre for Health Economics.

42 Rawson, Nigel SB (2020). Fewer new drug approvals in Canada: early indications of unintended consequences from new patented medicines regulations. Canadian Health Policy, March 2020. <https://www.canadianhealthpolicy.com/products/fewer-new-drug-approvals-in-canada--early-indication-of-unintended-consequences-from-new-pmprb-regs-.html>

43 Skinner, Brett J. Consequences of over-regulating the prices of new drugs in Canada. Canadian Health Policy, March 27, 2018. <https://www.canadianhealthpolicy.com/products/consequences-of-over-regulating-the-prices-of-new-drugs-in-canada.html>.

44 PMPRB (2017). Meds Entry Watch, 2015. Appendix, Figure I.1 Share of NASS launched by OECD country, Q4-2015. Based on the non-PMPRB external data source: MIDAS™ database, IMS AG. <http://www.pmprb-cepmb.gc.ca/view.asp?ccid=1307&lang=en>.

45 PMPRB (2016). 2015 Annual Report. Figure 10. Average Foreign-to-Canadian Price Ratios, Patented Drugs, OECD, 2015.

46 OECD (2017). Gross domestic product (GDP) (indicator). (Accessed on 12 October 2017). Population (indicator). (Accessed on 23 October 2017). Organisation for Economic Co-operation and Development.

47 Canada Gazette Publications Part I: Vol. 151, No. 48 — December 2, 2017. Regulations Amending the Patented Medicines Regulations. REGULATORY IMPACT ANALYSIS STATEMENT.

48 Regulations Amending the Patented Medicines Regulations (2019). Page 5992.

49 Giaccotto et al (2005). Drug Prices and Research and Development Investment Behavior in the Pharmaceutical Industry. The Journal of Law & Economics, 48(1), 195–214.

50 Koenig and MacGarvie (2011). Regulatory policy and the location of bio-pharmaceutical foreign direct investment in Europe, Journal of Health Economics, Volume 30, Issue 5, 2011, Pages 950–965.

51 Rawson, Nigel SB (2020). Clinical Trials in Canada Decrease: A Sign of Uncertainty Regarding Changes to the PMPRB? Canadian Health Policy, April 2020. Toronto: Canadian Health Policy Institute. <https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada-decrease--a-sign-of-uncertainty-regarding-changes-to-the-pmprb-.html>

52 Rawson, Nigel SB (2021). Clinical Trials in Canada: Worrying Signs that Uncertainty Regarding PMPRB Changes will Impact Research Investment. Canadian Health Policy, February 2021. <https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada--worrying-signs-that-pmprb-changes-will-impact-research-investment.html>

53 Rawson, Nigel SB (2021). Clinical Trials in Canada: Worrying Signs Remain Despite PMPRB's Superficial Response. Canadian Health Policy, March 2021. <https://www.canadianhealthpolicy.com/products/clinical-trials-in-canada--worrying-signs-remain-despite-pmprb---s-superficial-response.html>

54 Skinner, Brett J. Patented drug prices and clinical trials in 31 OECD countries 2017: implications for Canada's PMPRB. Canadian Health Policy, August 2019.

<https://www.canadianhealthpolicy.com/products/patented-drug-prices-and-clinical-trials-in-31-oecd-countries-2017--implications-for-canada---s-pmprb-.html>.

55 PMPRB. 2017 Annual Report. Figure 21. Average Foreign-to-Canadian Price Ratios, Patented Medicines, OECD, 2017.

56 ClinicalTrials.gov. U.S. National Library of Medicine (NLM), National Institutes of Health (NIH). Data extracted: Aug 04, 2019.

57 OECD.Stat. Datasets: Economic References, Demographic References. Data extracted: Aug 04, 2019.

58 PMPRB. 2008 and 2017 Annual Reports. Tables 21 (2008) and 18 (2017).

59 IQVIA. The Global Use of Medicines in 2019 and Outlook to 2023. IQVIA Institute for Human Data Science. January 2019.

60 ClinicalTrials.gov. U.S. National Library of Medicine (NLM), National Institutes of Health (NIH). Data extracted: Aug 07, 2019.

61 US FDA. <https://www.fda.gov/patients/drug-development-process/step-3-clinical-research>.

62 Health Canada (2017). Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations. Page 3.

63 PMPRB (2016). PMPRB Guidelines Modernization: Discussion Paper. Page 6.

64 Health Canada (2017). Protecting Canadians from Excessive Drug Prices: Consulting on Proposed Amendments to the Patented Medicines Regulations. Page 3.

65 PMPRB (2016). PMPRB Guidelines Modernization: Discussion Paper. Page 6.

66 Patricia M. Danzon (2018). Differential Pricing of Pharmaceuticals: Theory, Evidence and Emerging Issues. *PharmacoEconomics*. <https://doi.org/10.1007/s40273-018-0696-4>.

67 Patricia Danzon, Adrian Towse, Jorge Mestre-Ferrandiz (2015). Value-Based Differential Pricing: Efficient Prices for Drugs in a Global Context. *Health Economics* 24: 294–301 (2015).

68 Lichtenberg, Frank R., Pharmaceutical Price Discrimination and Social Welfare. *Capitalism and Society*, Vol. 5, Issue 1, Article 2, 2010. Available at SSRN: <https://ssrn.com/abstract=2208666>.

69 PMPRB (2020). 2019 Annual Report. Page 46.

70 PMPRB (2020). 2019 Annual Report. Page 47.

71 PMPRB (2020). 2019 Annual Report. Page 47.

72 PMPRB (2020). 2019 Annual Report. Page 45.

73 PMPRB (2020). 2019 Annual Report. Patented Medicine Prices Review Board.

74 Skinner, Brett (2021). Prices for Patented Medicines in Canada and 13 Other Countries: Testing the PMPRB's Narrative Justification for Amending the Regulations. *Canadian Health Policy*, August 2021. www.canadianhealthpolicy.com

75 Health Canada (2017). Page 3.

76 PMPRB (2016). PMPRB Guidelines Modernization: Discussion Paper. Page 6.

77 Regulations Amending the Patented Medicines Regulations... Page 5948.

78 Regulations Amending the Patented Medicines Regulations... Page 5952-5954.

79 Canadian Health Policy Institute (CHPI). Facts about the cost of patented drugs in Canada: 2018 Edition. *Canadian Health Policy*, February 2019.

<https://www.canadianhealthpolicy.com/products/facts-about-the-cost-of-patented-drugs-in-canada--2018-edition-.html>

80 CIHI National Health Expenditure Trends, 2020 — Methodology Notes. Page 9, "Drugs".

81 Patented Medicine Prices Review Board. Annual Report 2019.

82 The latest data available cover the fiscal year 2018–19 excluding Quebec and Nunavut. CIHI Data tables: Trends in Hospital Spending, 2005–2006 to 2018–2019.

<https://www.cihi.ca/en/hospital-spending>

83 CHPI (2020). Patented Medicines Expenditure in Canada 1990-2019. *Canadian Health Policy*, June 2021. <https://www.canadianhealthpolicy.com/products/patented-medicines-expenditure-in-canada-1990-2019.html>

84 PMPRB Annual Report 2019. Figure 10.

85 Johannesson, M. et al. (2009), Why should economic evaluations of medical innovation have a societal perspective? OHE Briefing, No. 51, Office of Health Economics, London.

86 Canadian Health Policy Institute (CHPI). Evidence that innovative medicines improve health and economic outcomes: focused literature review. *Canadian Health Policy*, April 2019.

www.canadianhealthpolicy.com

87 Lichtenberg, Frank R (2016). The Benefits of Pharmaceutical Innovation: Health, Longevity, and Savings. Montreal Economic Institute. June 2016.

88 Lichtenberg FR (2015). The impact of pharmaceutical innovation on premature cancer mortality in Canada, 2000–2011. *International Journal of Health Economics and Management*. September 2015, Volume 15, Issue 3, pp 339-359.

89 Hermus G, Stonebridge C, Dinh T, Didic S, Theriault L (2013). Reducing the Health Care and Societal Costs of Disease: The Role of Pharmaceuticals. The Conference Board of Canada, July 2013.

90 Lichtenberg FR (2012). Pharmaceutical Innovation and Longevity Growth in 30 Developing and High-income Countries, 2000-2009. National Bureau of Economic Research (NBER), Working Paper No. 18235. July 2012.

91 Frank R. Lichtenberg, Paul Grootendorst, Marc Van Audenrode, Dominick Latremouille-Viau, Patrick Lefebvre (2009). The Impact of Drug Vintage on Patient Survival: A Patient-Level Analysis Using Quebec's Provincial Health Plan Data. *Value in Health*, Volume 12, Number 6, 2009.

92 Pierre-Yves Crémieux et al (2005). Public and Private Pharmaceutical Spending as Determinants of Health Outcomes in Canada. *Health Economics*, Vol. 14, No. 2, February 2005, pp. 107-116.

93 Lichtenberg FR (2002). Benefits and Costs of Newer Drugs: An Update. National Bureau of Economic Research (NBER), Working Paper No. 8996. June 2002.

94 Canadian Health Policy Institute (CHPI). Evidence that innovative medicines improve health and economic outcomes: focused literature review. *Canadian Health Policy*, April 2019. www.canadianhealthpolicy.com.

95 Gowlings WLP (2021). Only the Excess – Federal Court of Appeal Criticizes PMPRB for Engaging in Consumer Protection. 04 August 2021. <https://gowlingwlg.com/en/insights-resources/articles/2021/federal-court-appeal-pmprb-consumer-protection/>

96 PMPRB (February 9, 2021). Communications Plan. Posted by CORD: <http://www.raredisorders.ca/content/uploads/file-2.pdf>

97 Globe and Mail. Is Ottawa prepared to call Big Pharma's bluff? Konrad Yakabuski (June 4, 2021).

98 Canadian Organization for Rare Disorders (CORD) (2021). PMPRB Campaign to Discredit Patients and Others Who Do Not Agree with Them. <https://www.raredisorders.ca/5045-2/>

99 Savoie (2021). Report of Donald J. Savoie on Machinery of Government Issues with respect to the Patented Medicine Prices Review Board, June 7, 2021. <http://www.raredisorders.ca/content/uploads/Savoie-DJ-re-PMPRB-and-Duty-of-Neutrality-June-7-2021.pdf>

100 Savoie (2021). Page 3.