# PMPRB written response to questions from the House of Commons Standing Committee on Health on November 23 and 27, 2020

Submitted on December 11, 2020

Patented Medicine Prices Review Board
Conseil d'examen du prix des médicaments brevetés

Canada

**QUESTION 1**

*Third party analysis ("CONECTed") shows that only 4 out of 6 new cancer drugs analyzed would not come to Canada based on June Guidelines. And even based on Nov. Guidelines, still 2 of them would not come. Do you agree with that?*

**MP Theriault**

## PMPRB Answer

- All six of these oncology medicines are currently marketed in Canada.

- CONECTed's original analysis, based on the November 2019 draft Guidelines, found that only 2 of the 6 medicines would be likely to launch under the PMPRB's new regulatory framework.

- CONECTed shared this analysis with the PMPRB during a consultation meeting on February 13, 2020 and memorialized it in their written submission.

- In response to concerns of this kind articulated by CONECTed and like-minded stakeholders, the PMPRB issued a second draft of the Guidelines in June 2020 which introduced (i) higher pharmacoeconomic value thresholds (from $60K to up to $200K), (ii) caps on the price reductions required by the new economic factors, and (iii) application of these only for sales exceeding $12M annually. These were some of several major changes brought to the Guidelines over the course of a year-long consultation process.

- In its follow up submission in response to the June 2020 draft Guidelines, CONECTed concluded that all 6 medicines would now be likely to have launched in Canada as a result of these changes: *"Overall, given anecdotal evidence of the price reductions sought by the pCPA, these potential price reductions appear manageable and, thus it appears the MRP calculation algorithms themselves may have been unlikely to affect a launch decision had the 2020 draft Guidelines been in place at the time of the launch of*" [the medicine analyzed]. The results of the CONECTed analysis are summarized in Table 1.

Table 1. Likelihood of launch under the PMPRB draft Guidelines, select oncology medicines

| Molecule | Trade Name | November Draft | June Draft |
|---|---|---|---|
| venetoclax | Venclexta | Very Unlikely | Likely |
| nivolumab | Opdivo | Likely | Likely |
| daratumumab | Darzalex | Very Unlikely | Likely |
| blinatumomab | Blincyto | Very Unlikely | Likely |
| dinutuximab | Unituxiini | Very Likely | Likely |
| osimertinib | Tagrisso | Very Unlikely | Likely |

Source of information: CONECTed submissions to PMPRB November and June Guideline consultation

- However, in their latest brief to HESA, CONECTed now states that only 4 of 6 medicines would have been likely to have launched in Canada under the Guidelines. Despite referencing a supporting analysis, no such analysis is included in, or appended to, the brief. As a result, we are unable to understand the basis for this disconnect between CONECTed's most recent submission to the PMPRB and its HESA brief.

**QUESTION 2**

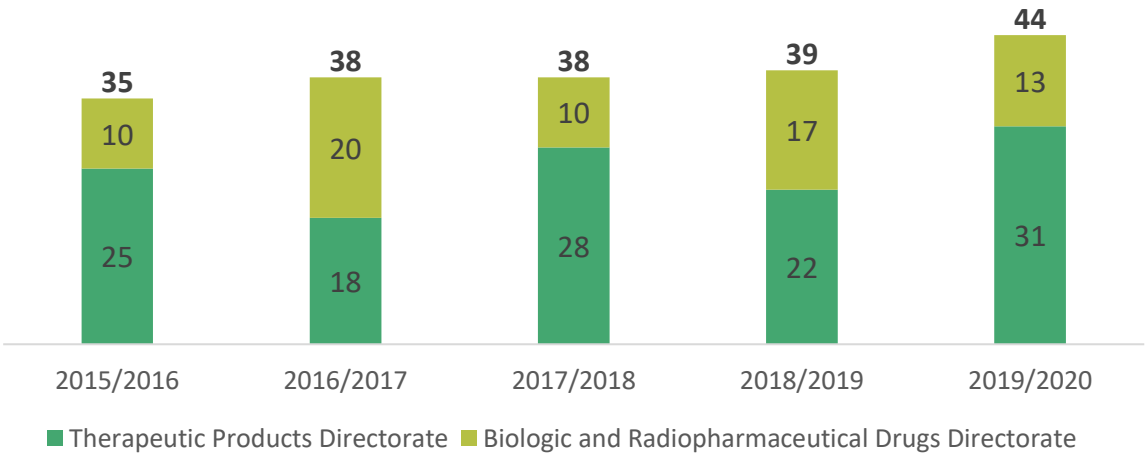
*This year we see 40% drop of the applications [to Health Canada for approval to market a new drug]. From 2018 PMPRB annual report we also see drop of patented sales share [of total pharmaceutical expenditures]…do you have 2019 PMPRB annual report and what does it look like?*

**MP Kmiec**

**PMPRB** **Answer**

- In response to the recent regulatory amendments, some stakeholders are suggesting that manufacturers have responded by reducing the number of drug launches in Canada.
- A review of the data by the PMPRB has not found any evidence to substantiate this claim.
- In terms of the number of new drug applications, according to the most recent information reported by Health Canada, the number of submissions seeking approval to market new innovative medicines in Canada (aka "New Active Substances "NAS") in 2019-20 increased to 44, well above the 37.5 average from 2015-16 to 2018-19 (Figure 1).

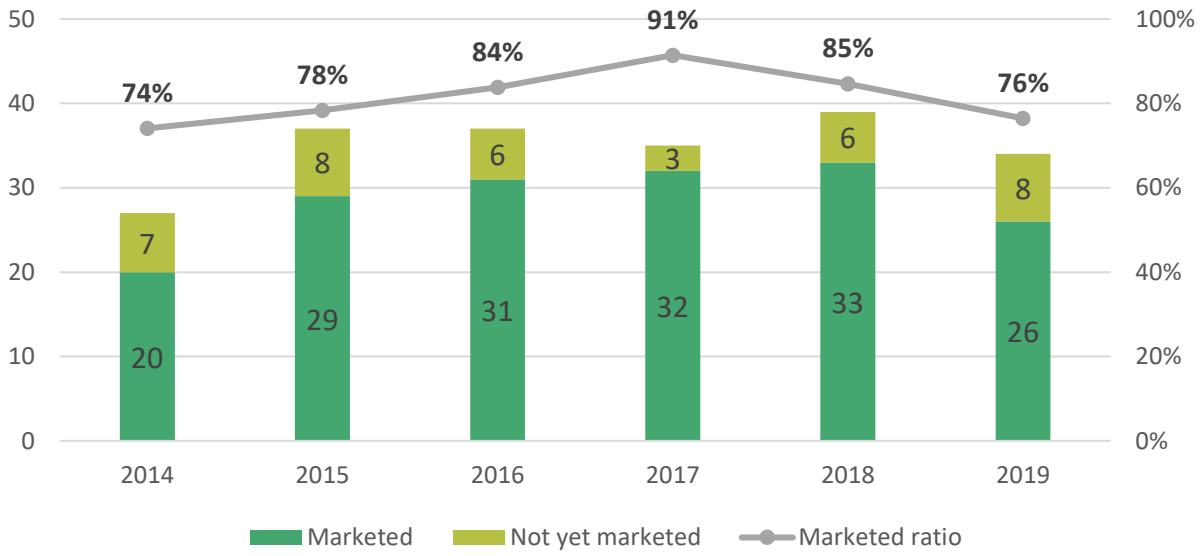
Figure 1. Health Canada Submissions Received – New Active Substances




Data Source: Biologic and Radiopharmaceutical Drugs Directorate: Drug Submission Performance Annual Report Fiscal Year 2019-2020 NDS
Therapeutic Products Directorate: Drug Submission Performance Annual Report Fiscal Year 2019-2020 NDS

- The PMPRB analysis of the Health Canada drug product database indicates that the number and share of medicines approved in 2019 and marketed by the 3rd quarter of the following year (2020) is within the range observed for the previous five years. This suggests that a comparable number and share of new drugs approved in Canada in 2019 were commercialized.

Figure 2. Number of marketed versus approved new medicines* in Canada, 2014 to 2019




Data source: Health Canada Drug Product Database
* By the third quarter of the following year

- At Health Canada's 2020 Virtual Stakeholder Meeting on Health Products, which took place on Friday, December 4, 2020, Pierre Sabourin, the Assistant Deputy Minister of the Health Products and Food Branch, confirmed that the department received the "same number" of applications for NAS's in 2020 as in the previous year.

- According to the PMPRB's latest calculations, which will be included in its upcoming 2019 Annual Report to be tabled in Parliament, patented medicines accounted for a 60% share of total pharmaceutical expenditures in Canada in 2019, which is unchanged from the previous year.

- The 2019 Annual Report has not yet been submitted to the Minister of Health for tabling in Parliament. The final draft of the document in English is completed and we are awaiting the French translation before sending it to the Minister of Health for tabling.

**QUESTION 3**

*How was that $12M threshold set? Would you be able to provide that ICER report to the Committee?*

**MP Kmiec**

**PMPRB** **Answer**

- The $12 million threshold is based on the average annual affordability threshold per medicine in Canada, which was discussed in the PMPRB Backgrounder document accompanying the November draft Guidelines. The methodology used is similar to that of the Institute for Clinical and Economic Review (ICER) in the United States. The ICER report that explains the methodology is publicly available.

- A growth in the sales for the patented medicine in Canada that would be in line with the above assumptions would result in an annual increase in patented medicine sales of $432M. Considering that there are on average 36 new patented medicines introduced every year to absorb this growth, it would mean that each medicine would generate on average $12M in patented drug sales, as shown in Table 2.

Table 2. Estimated average annual affordability threshold per medicine in Canada

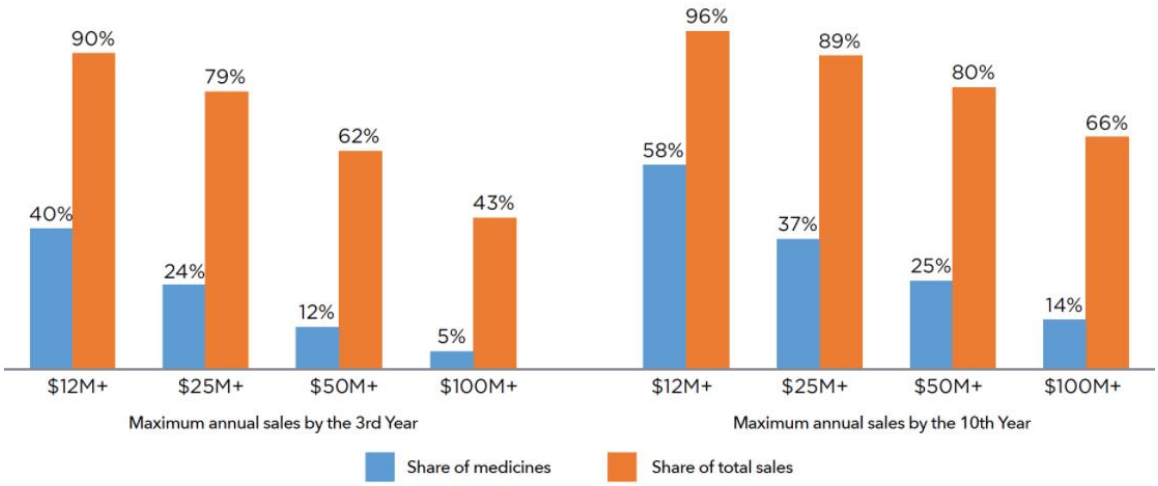
| | |
|---|---|
| Average annual patented medicines sales, 2014 to 2018 ($B) | $14.9B |
| Average annual growth in patented medicine sales, in line with the growth rate in GDP | $432M |
| Average number of new patented medicines introduced per year, 2014 to 2018 | 36 |
| Average annual affordability threshold per medicine | $12M |

Source: PMPRB Backgrounder – November draft Guidelines

- Medicines that cost over $90,000 annually (i.e., high cost "Category 1" medicines) that realize less than $12M in annual revenue will not be subject to the lower Maximum Rebated Price (MRP) ceiling resulting from the application of the new economic factors. This will ensure that medicines which treat rare diseases are not discouraged from coming to Canada out of concern that their net price will be substantially reduced by the application of the new economic factors.

- The most recent available data suggests that a sizable portion of patented medicines (42.5%) do not realize $12M in annual revenues in any of the first 10 years on the market (Figure 2). These medicines only accounted for 3.7% of patented sales, suggesting that even cumulatively these medicines do not give rise to affordability concerns.

Figure 3. Patented medicines in Canada, share of medicines and share of sales, by maximum annual sales




Source: PMPRB Backgrounder – June draft Guidelines
Data source: PMPRB, 2018; CPI applied to bring historical sales into 2018 value
*Included patented drugs launched after 1998 in Canada; Sample Size: N=639 for the 3-year analysis; N=338 for the 10-year analysis

**QUESTION 4**

*What is the exact portion (of the total pharmaceutical expenditures annually) that is spent annually on medicines for rare diseases?*

**MP Theriault**

**PMPRB** **Answer**

- The Canadian Forum for Rare Disease Innovators (RAREi) hired Patient Access Solutions (PAS) to review the PMPRB's analysis of spending on expensive drugs for rare diseases (EDRD). In conducting that analysis, PAS removed drugs that treat rare forms of cancer from its calculated total of annual spending on EDRDs on the premise that oncology drugs skew the results towards drugs with additional indications that drive up expenditure.

- In addition to excluding expensive drugs for rare forms of cancer, the PAS study limited its analysis to drugs for rare diseases that are approved and funded by public drug programs. It therefore does not account for expenditures incurred by other payers in the Canadian market. It will be recalled that public payers account for a minority (42%) of total pharmaceutical spending in Canada.

- Based on the above described analysis, PAS found that the total annual expenditures on drugs for rare diseases in Canada in 2019 was $280 million, representing 2% of total spending on medicines in Canada.

- The PMPRB has conducted its own analysis on the national expenditures related to EDRDs. The PMPRB's definition of EDRD encompasses medicines that have received an orphan indication and cost at least $100,000 per year for non-oncology and $7,500 or more per 28-day cycle for oncology drugs. The PMPRB included in its analysis both oncology and non-oncology medications, as drugs that treat rare forms of cancers are also considered drugs for rare diseases. The result of that analysis shows that in 2019 total expenditures on EDRDs in Canada was $2.5 billion in Canada.

- EDRDs are the fastest growing market segment of the pharmaceutical market in Canada, growing at an annualized rate of 32%. Despite their small number, EDRDs account for nearly one-tenth of pharmaceutical sales (10.3% in SA2-2020), with the majority of sales

coming from oncology medicines (7.7%) and the remaining 2.6% from non-oncology medicines.

- It is important to understand that many new EDRDs are initially approved to treat a rare or orphan disease that will result in a limited number of sales because of the small patient population but eventually obtain approval to treat additional diseases such that their market size expands exponentially. This phenomenon is not limited to non-oncology EDRDs, which is a further reason why the PMPRB has not exempted high cost medicines that realize annual revenues above $12M from the application of the new economic factors.

- The PMPRB's recognition that medicines for rare disease include rare cancers is aligned with that of the World Health Organization, which in its *Technical report: pricing of cancer medicines and its impacts*, acknowledges that "*governments have implemented a range of policy incentives to stimulate the R&D of medicines for rare diseases, including rare cancers*".

**QUESTION 5**

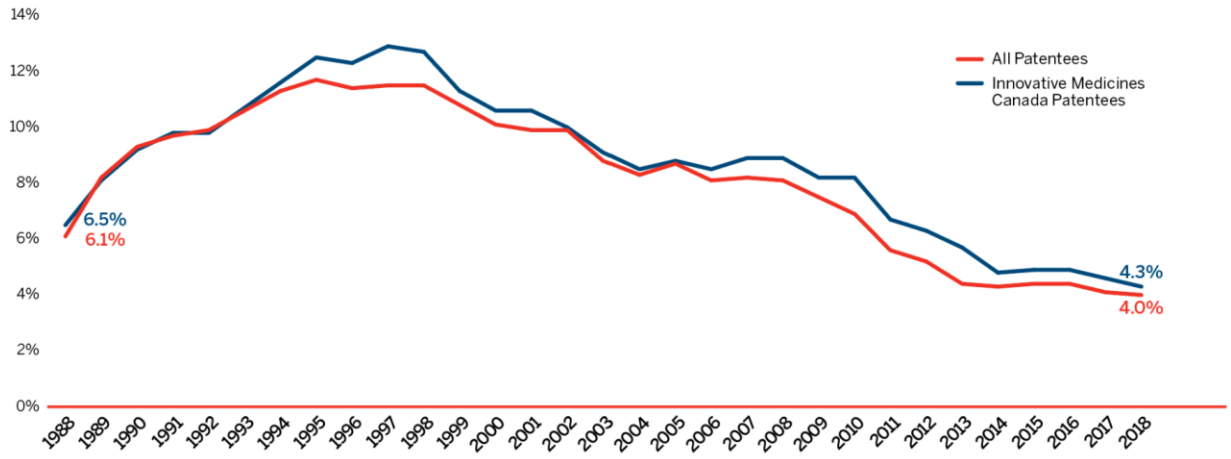
*Will the proposed PMPRB regulatory changes result in less pharmaceutical research and development in Canada?*

**MP Davis**

**PMPRB** **Answer**

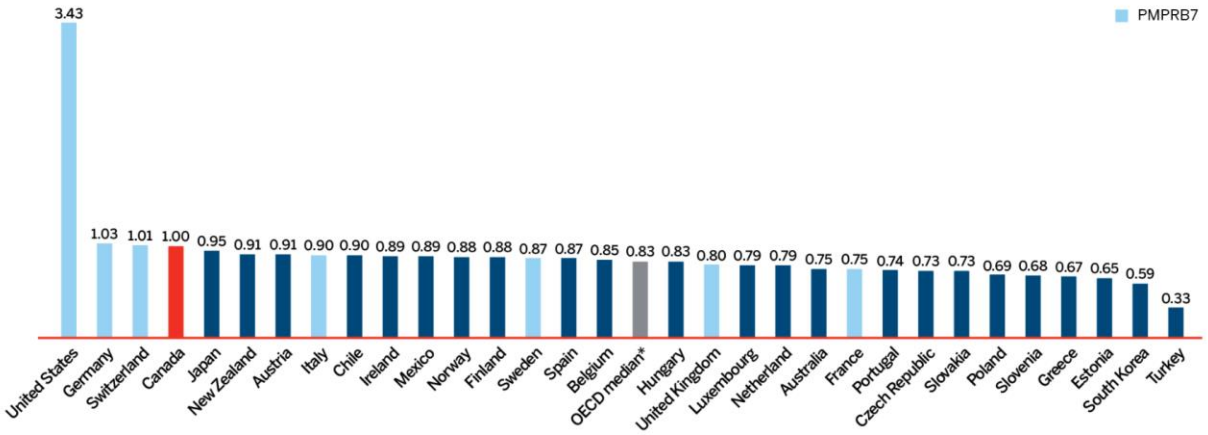
- Despite Canada having the fourth highest prices (Figure 4), and the second highest spending per capita (Figure 5) on patented medicines among the OECD countries, the percentage of research and development (R&D)-to-sales by pharmaceutical patentees in Canada has been falling since the late 1990's and has been under the agreed-upon target of 10% since 2003 (Figure 3). In 2018, it was at 4.0% for all patentees lower than 30 years ago when patent protection for medicines was strengthened and the PMPRB was created to protect consumers from excessive pricing.

Figure 4. R&D-to-Sales Ratio, Pharmaceutical Patentees, 1988 to 2018




Source: PMPRB Annual Report 2018
Data source: PMPRB

Figure 5. Average Foreign-to-Canadian Price Ratios, Patented Medicines, OECD, 2018

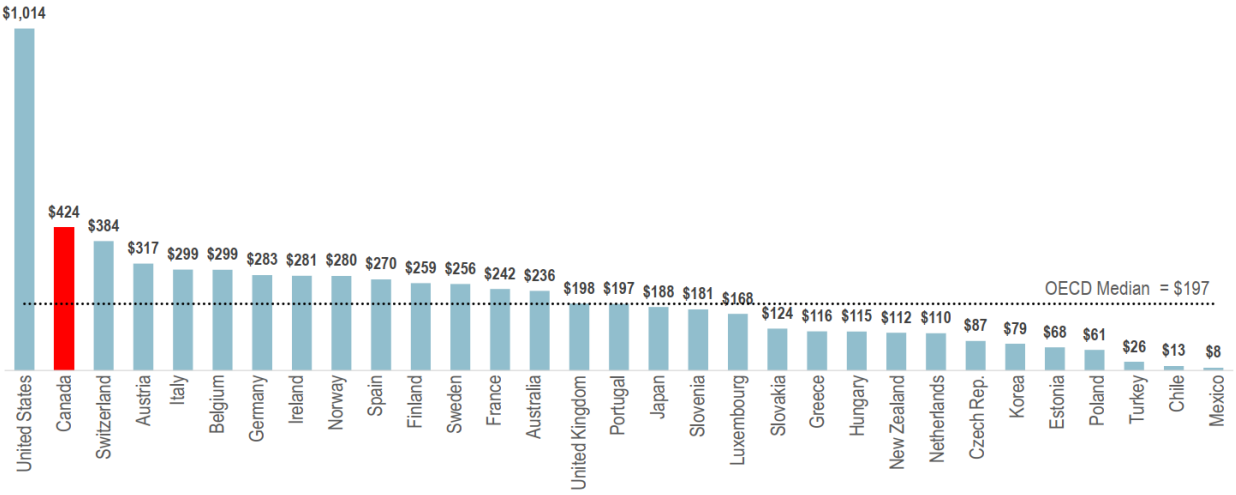



Source: [PMPRB Annual Report 2018]

Data source: MIDAS® database, 2018, IQVIA (all rights reserved)

Note: Calculated at Medicine Level for medicines with prices available in at least three foreign markets

Figure 6. Patented Medicine Spending Per Capita, OECD Countries, 2018




Source: [PMPRB Research Webinar 2: July 6]

Data source: IQVIA MIDAS® 2018 (Patented Spending); OECD (population)

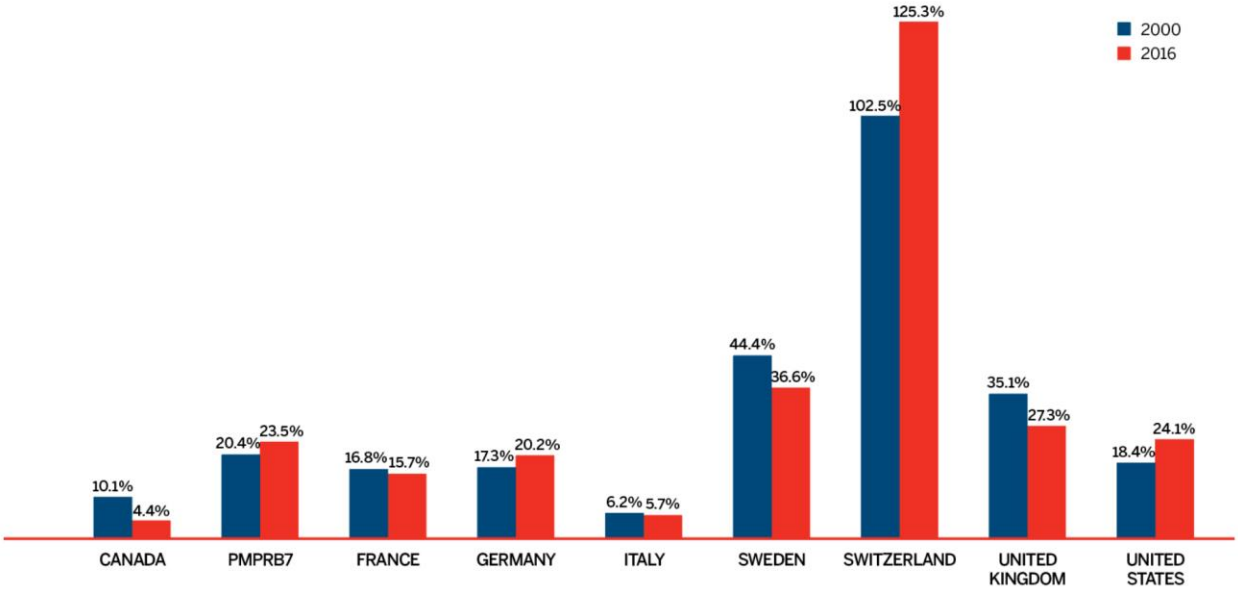
Note: Patented medicines were identified based on patents in Canada, for which sales were extracted for other countries. Spending data for Greece, Chile, Estonia, Luxembourg and Mexico include only retail sales. and exclude hospital sales. Includes only countries for which data are available.

- Empirical evidence does not support the claimed link between drug pricing and the level of R&D investment in a country. In fact, most of Canada's peer countries enjoy far greater levels of R&D investment despite having considerably lower prices (Figure 6 and Figure 7).

- Belgium enjoys 20 times more R&D investment dollars per resident than Canada despite the fact that Belgian prices are 21% lower than Canadian prices (2017).

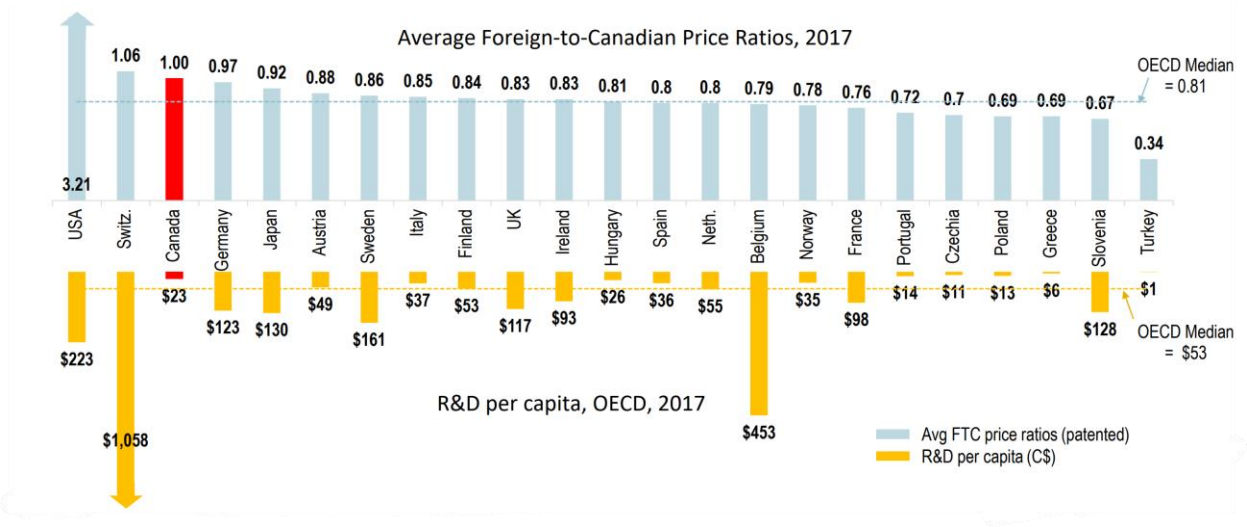
- France enjoys over 4 times more R&D investment dollars per resident than Canada despite the fact that French prices are 24% lower than Canadian prices (2017).

Figure 7. R&D-to-Sales Ratios, Canada and the PMPRB7




Source: PMPRB Annual Report 2018
Data Source: PMPRB; European Federation of Pharmaceutical Industries and Associations (EFPIA): the Pharmaceutical Industry in Figures 2017; PhRMA 2017 profile

Figure 8. Average foreign-to-Canadian Price Ratios versus R&D per capita in the OECD, 2017




Source: PMPRB Research Webinar 2: July 6
Data source: PMPRB (FTC, R&D); OECD (population)
Note: Total R&D investments, e.g. by patentees, other companies, universities, hospitals, other.

**QUESTION 6**

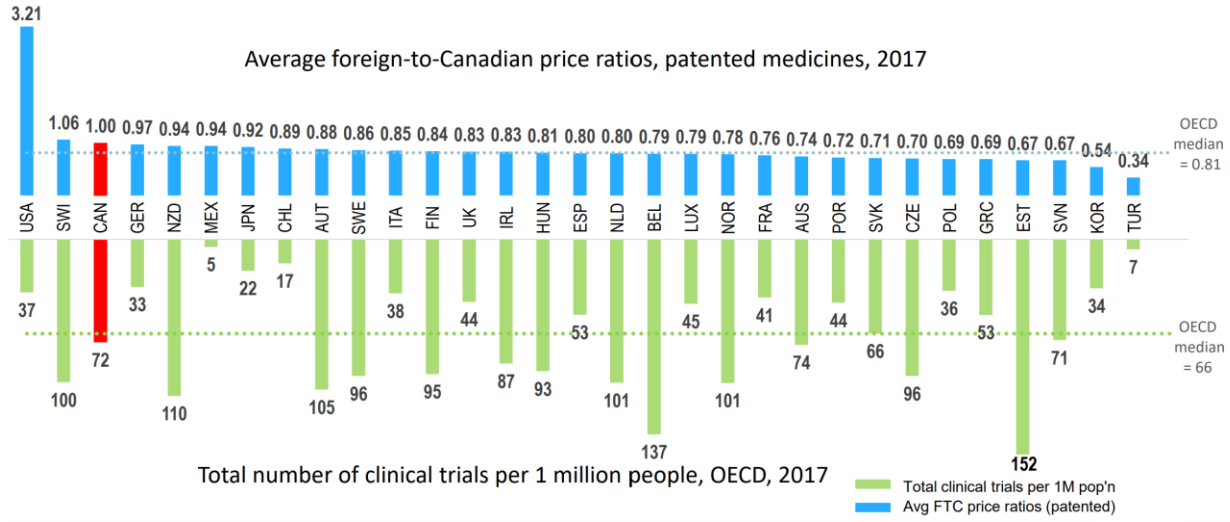
*Will the proposed PMPRB regulatory changes result in fewer clinical trials in Canada?*

**MP Davis**

**PMPRB** **Answer**

- Lower prices do not generally result in a lower number of clinical trials. Many countries with lower patented medicine prices than Canada have a higher number of clinical trials per 1 million people (Figure 8).

Figure 9. Average foreign-to-Canadian price ratios versus total number of clinical trials per 1 million people, OECD, 2017




Source: PMPRB Research Webinar 2: July 6
Data source: PMPRB Annual Report 2017; GlobalData®; OECD (population).

- Industry-sponsored studies that claim a dramatic decline in the number of clinical trials recently are based on incomplete databases that account for only a subset of total clinical trials in Canada (i.e. Health Canada's Clinical Trial Database) and do not account

for the considerable lag time between the issuance by Health Canada of "No-Objection Letters" and their inclusion in the Clinical Trial Database.

- Accordingly, the most recent quarters in any given time period will always show a significantly lower number of clinical trials than earlier quarters, owing to the lag time in updating the database.

- For example, a snapshot of the number of trials in the spring of 2020 for which Health Canada issued a No-Objection Letter would suggest a dramatic drop in the number of clinical trials in the closing months of 2019 and the early months of 2020, as compared to the historical average (Table 3)

Table 3. Monthly number of Canadian clinical trials with " No Objection Letter", as of April 2020

| | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2020** | **15** | **27** | **24** | | | | | | | | | |
| **2019** | 41 | 54 | 57 | 72 | 70 | 41 | 67 | 39 | 44 | 54 | **21** | **34** |
| **2018** | 32 | 47 | 50 | 31 | 54 | 71 | 75 | 67 | 66 | 56 | 64 | 71 |

Data source: Health Canada Clinical Trial Database

- However, if one were to look at the data for November 2019 to February 2020, in the fall of 2020, a much different picture emerges: the number of clinical trials for the closing months of 2019 and the early months of 2020 rebound to normal levels, while the more recent months report a marked decline (Table 4). It is expected however that in due course, the numbers for these months will align with the historical average.

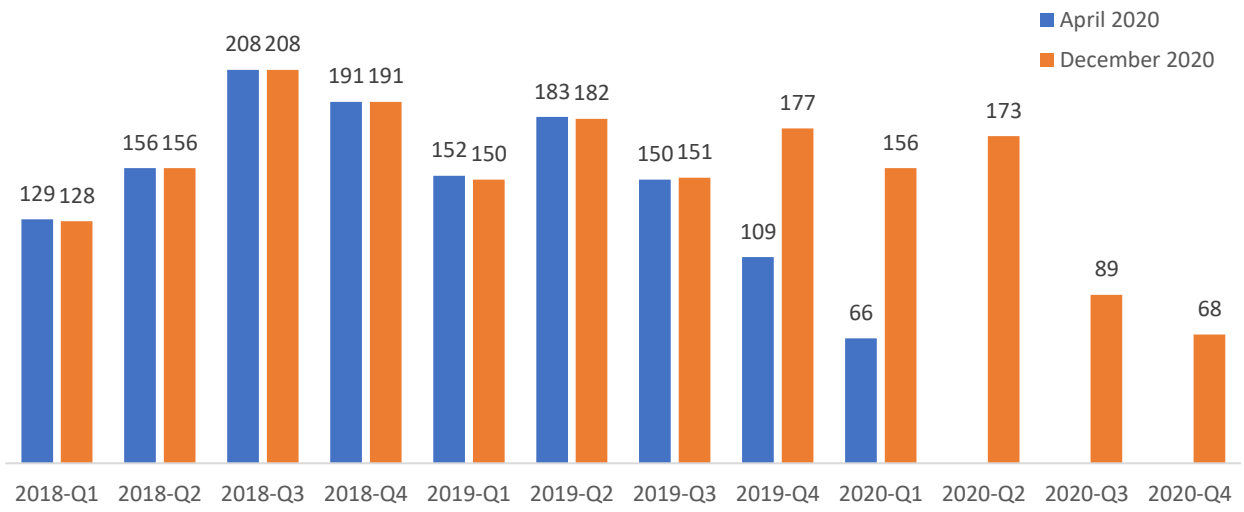
Table 4. Monthly number of Canadian clinical trials with " No Objection Letter", as of December 2020

| | Jan | Feb | Mar | Apr | May | Jun | Jul | Aug | Sep | Oct | Nov | Dec |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **2020** | **31** | **57** | **60** | 67 | 52 | 54 | 54 | 11 | 24 | 30 | 38 | 8 |
| **2019** | 40 | 53 | 57 | 72 | 70 | 41 | 67 | 39 | 44 | 54 | **47** | **76** |
| **2018** | 31 | 47 | 50 | 31 | 54 | 71 | 75 | 67 | 66 | 56 | 64 | 71 |

Data source: Health Canada Clinical Trial Database

- This lag time phenomenon is easily discoverable and any analysis of recent trends in clinical trial intensity in Canada that does not account for it is fundamentally flawed and misleading.

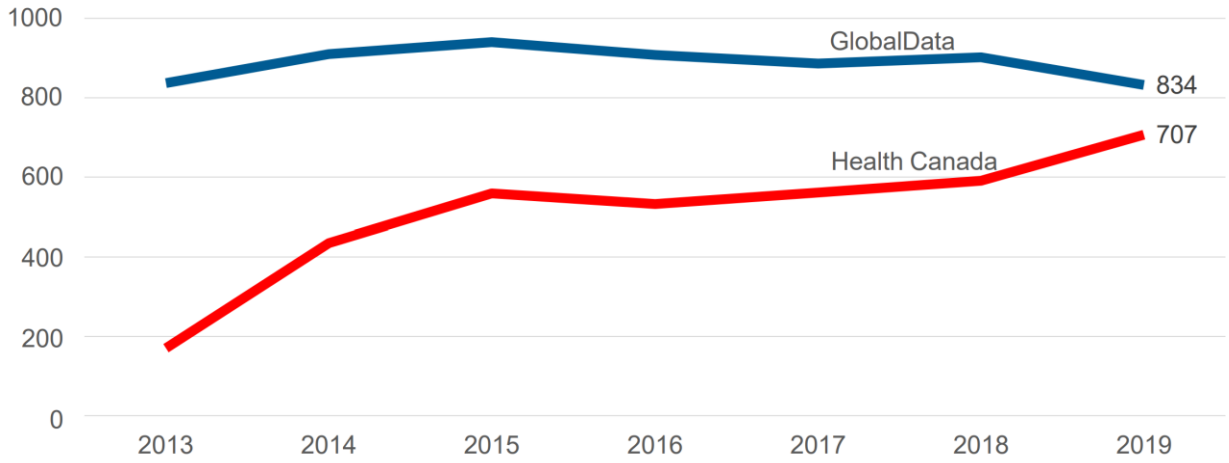
Figure 10. Quarterly number of Canadian clinical trials with " No Objection Letter", as of April 2020 versus December 2020 snapshot




Data source: Health Canada Clinical Trial Database

- While results based on Health Canada's Clinical Trial Database suggest that the number of new trials in on the rise in Canada, this database is not a registry, and is in fact a subset of all the clinical trials taking place in Canada.

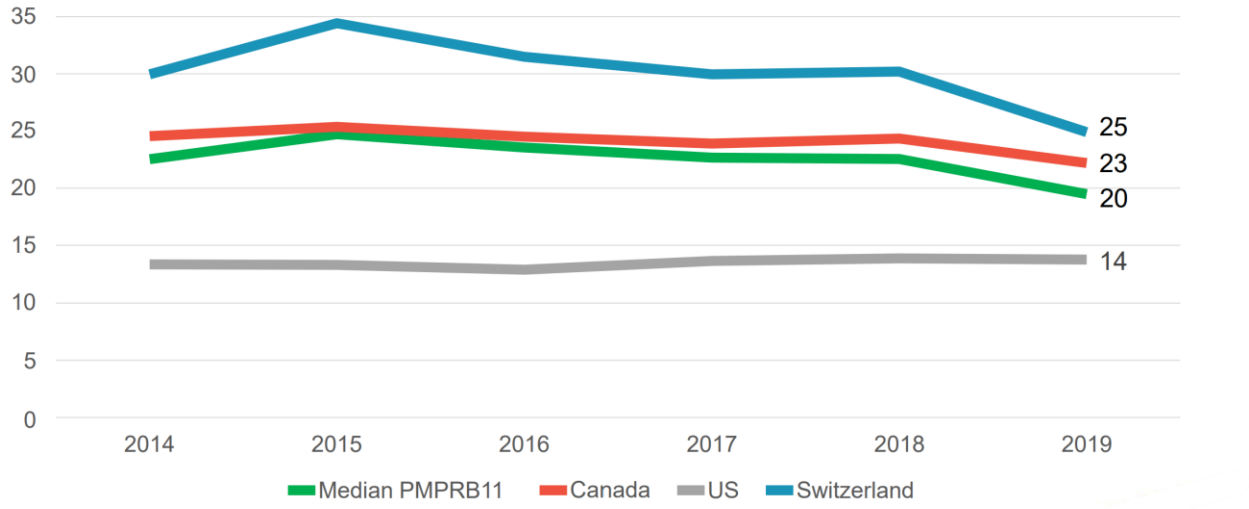
Figure 11: Number of new clinical trials by data source, 2013 to 2019




Source: PMPRB Research Webinar 2: July 6
Data source: GlobalData®; Health Canada Clinical Trial Database

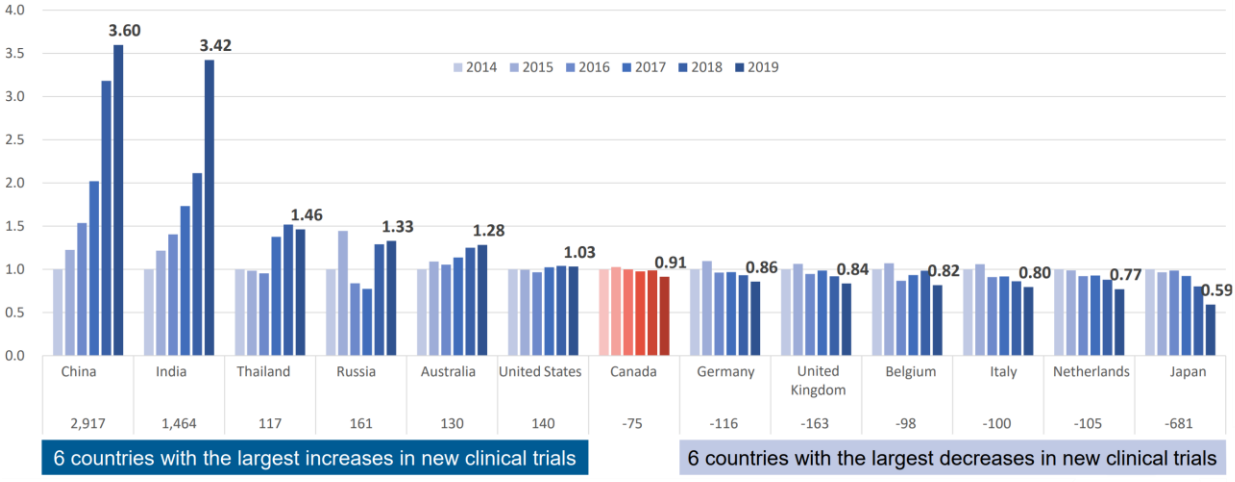
- The reality is that the number of clinical trials has been declining in recent years in developed countries as the pharmaceutical industry shifts its focus to emerging markets. In addition, it is widely reported and recognized that COVID-19 has disrupted clinical trial intensity globally in 2020 (Figure 11 and Figure 12). According to GlobalData, over 1,026 clinical trials globally are currently delayed or cancelled and another 880 clinical trials have resumed following a delay due to the COVID-19 pandemic.

Figure 12. Number of new clinical trials per 1 million people, 2014 – 2019




Source: PMPRB Research Webinar 2: July 6
Data source: GlobalData®

Figure 13. Index in new clinical trials for major markets, 2014 – 2019




Source: PMPRB Research Webinar 2: July 6
Data source: GlobalData®

**QUESTION 7**

*Generally, what percentage of research dollars that go into patented medicines are publicly funded?*

**MP Davis**

**PMPRB** **Answer**

- It is a generally accepted proposition that governments provide most of the funding for basic research. "Governments mainly support basic and early-stage research. Such funding is made through direct budget allocations, research grants, publicly-owned research institutions and funding of higher education institutions. The pharmaceutical industry translates and applies knowledge generated by basic research to develop products, and invests in large clinical trials required to gain market approval. The industry also receives direct R&D subsidies or tax credits in many countries". (Source)

- In 2009, it was estimated that globally 30% of the investments in health R&D (basic and applied) came from the public sector. The largest public funder was the United States National Institutes of Health ($26.1 billion), followed by the European Commission ($3.7 billion), and the United Kingdom Medical Research Council ($1.3 billion). (Source)

- Research in the US indicates that the National Institute of Health funding contributed to published research associated with every one of the 210 new drugs approved by the Food and Drug Administration from 2010–2016 (Source 1, Source 2).

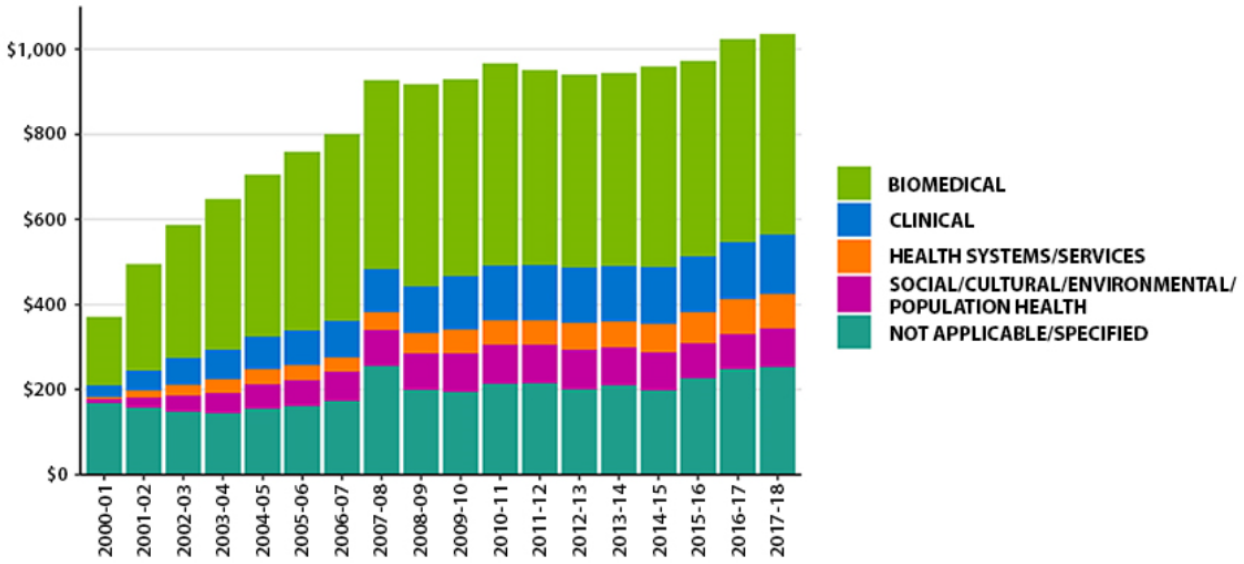
- Canada has strong financial support for health research. In 2016, the Canadian Institutes of Health Research (CIHR), Canada's federal funding agency for health research, which is composed of 13 virtual Institutes, supported thousands of health researchers across Canada, and provided close to $981 million in funding. In addition, Canada's provinces and territories, as well as private and not-for profit organizations, provide additional sources of funding to the sector. (Source)

- Canada also provides company-level funding support for health research. The National Research Council's Industrial Research and Assistance Program (NRC-IRAP) provides direct technology assistance to small and medium-sized enterprises, including life science companies, at all stages of the innovation process and provides linkages to the best expertise in Canada. Export Development Canada (EDC) and the Business Development Bank of Canada (BDC) provide flexible financing programs and solutions tailored to support foreign direct investment in Canada. (Source)

- The Canadian Institutes of Health Research (CIHR) is the largest funder of health research in Canada, supporting over 13,000 world-class researchers from all pillars of health research and from all regions of Canada. (Source)

- CIHR invested $472 million in biomedical health research and $140 million in clinical research in 2017/18, with the two components representing more than half of the $1 billion spent by CIHR in Canada on health research (Figure 13 and Figure 14). (Source)

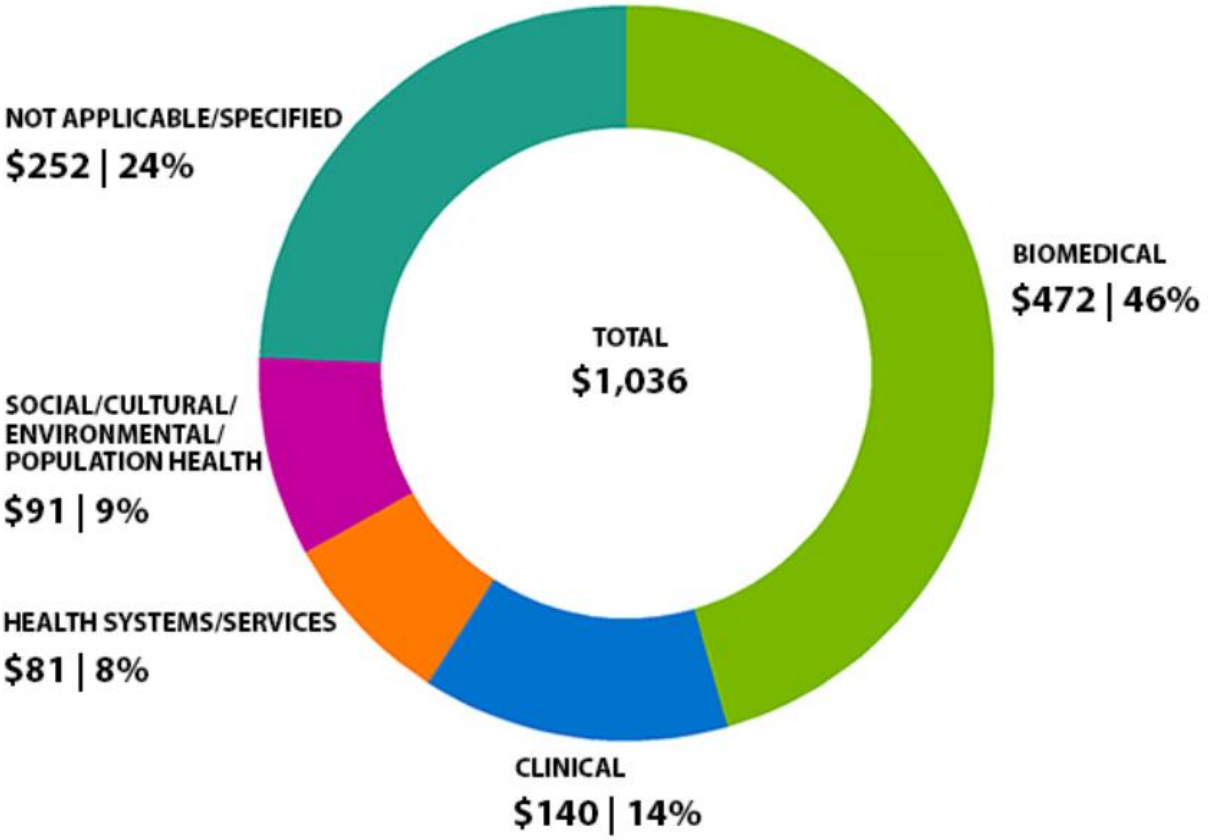
Figure 14: CIHR Fiscal Year Investments by Primary Theme since 2000–01 (in millions of dollars)




- Due to rounding, figures may not reconcile with other published information
- Excludes operating expenditures and partner contributions
- Primary theme designation is determined by the grantee at the time of application

Source: CIHR

Figure 15: CIHR Investments by Primary Theme 2017–18 (in millions of dollars)

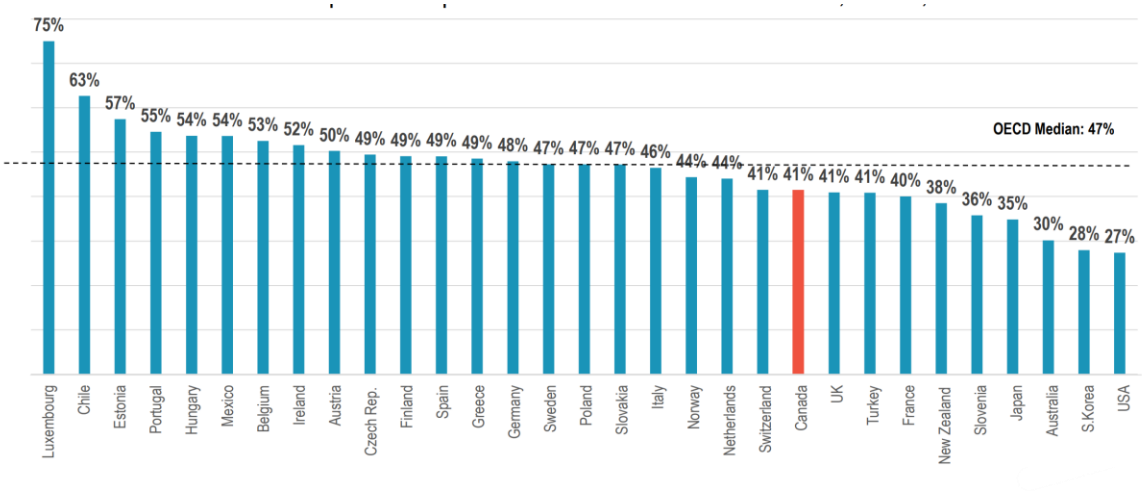



- Due to rounding, figures may not reconcile with other published information
- Excludes operating expenditures and partner contributions
- Primary theme designation is determined by the grantee at the time of application

Source: CIHR

- In Canada, only 41% of all new clinical trials are sponsored by pharmaceutical patentees, well below the OECD median of 47%. The majority of the clinical trials in Canada are sponsored by industry non-patentees (30%) and Institutions/Government (29%).

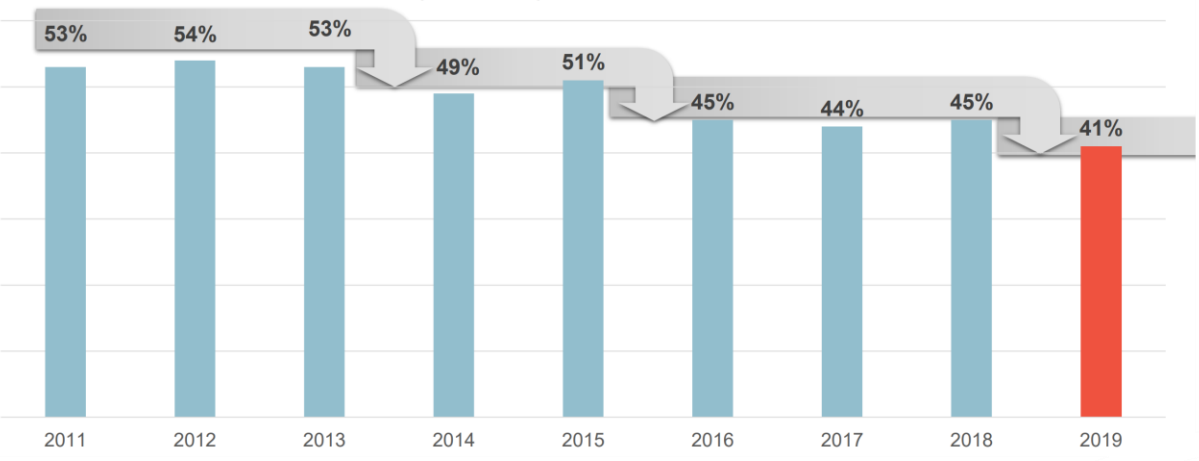
Figure 16. Share of new patentee-sponsored clinical trials: Phases 1 to 3, OECD, 2019




Source: PMPRB Research Webinar 2: July 6
Data source: PMPRB Annual Report 2017; GlobalData®

- While over half of all new clinical trials commenced in Canada were sponsored by pharmaceutical patentees earlier in the decade, by 2019 the share has dropped to 41%.

Figure 17. Share of new patentee-sponsored clinical trials: Phases 1 to 3




Source: PMPRB Research Webinar 2: July 6
Data source: PMPRB Annual Report 2017; GlobalData®