

# **The Real Story Behind Big Pharma's R&D Spending in Canada**

**Canadian Generic Pharmaceutical Association**

**2007**

**GENERIC DRUGS.**



**SAME QUALITY. LOWER PRICE.**

**Canadian Generic Pharmaceutical Association**

4120 Yonge Street, Suite 409, Toronto ON M2P 2B8 Tel: (416) 223-2333 [www.canadiangenerics.ca](http://www.canadiangenerics.ca)

## ***Table of Contents***

	<b>Page</b>
<b>The Real Story Behind Big Pharma’s R&amp;D Spending in Canada.....</b>	<b>1</b>
Dr. Marcia Angell on Big Pharma’s \$800-million per drug figure.....	1
Big Pharma breaking its R&D commitment to Canadians.....	2
Expenditure by type of research.....	2
Less than 2% of sales revenue spent on basic research.....	2
R&D Expenditure by Type of Research, 1988-2006.....	2
Clinical trials account for nearly 80% of applied research.....	3
Canada’s pharmaceutical R&D spending well behind other countries.....	3
R&D-to-domestic-sales ratios, Canada and 7 Comparator countries,.....	3
2000 and 2004	
Most “new” drugs not truly innovative.....	4
Taxol: A Case Study on Big Pharma’s “Innovation”.....	5
Increased patent protection has not resulted in increased R&D spending.....	6
Generic Pharmaceutical R&D Spending in Canada Outpaces Brands’.....	6
Pharmaceutical Industry Investment in Canada: Generic vs. Brand.....	7
Canada’s Trade Deficit in Pharmaceutical and Medicine Manufacturing.....	7
Longer market monopolies through increased “data exclusivity”.....	8
Six-month pediatric exclusivity.....	9
Conclusion.....	9

### **Canadian Generic Pharmaceutical Association**

4120 Yonge Street, Suite 409  
Toronto, Ontario M2P 2B8  
Tel: (416) 223-2333  
Fax: (416) 223-2425  
Email: [info@canadiangenerics.ca](mailto:info@canadiangenerics.ca)  
Website: [www.canadiangenerics.ca](http://www.canadiangenerics.ca)

**GENERIC DRUGS.**



**SAME QUALITY. LOWER PRICE.**

## The Real Story Behind Big Pharma's R&D Spending in Canada

The mantra of the brand-name pharmaceutical industry is that without higher prices and extraordinary rules like the *Patented Medicines (Notice of Compliance) Regulations* and increased data protection provisions there will not be enough profit to recoup investments in research and development.

**“Sales and marketing spend is running at roughly twice that of R&D spend. This ratio is making it quite difficult to use the R&D argument successfully.”**

AstraZeneca CEO Tom McKillop, *The Pink Sheet*, November 22, 2004

In fact, the lobby group for the brand-name industry in Canada claims that the average cost to develop a new medicine is \$1.3 billion. This figure is a conversion to Canadian dollars from the US\$800 million figure used by the brands in the United States.

One of the most commonly cited sources for this figure is a November 2001 report from the Tufts Center for the Study of Drug Development, which receives 65% of its funding from drug companies. (*Comparing Facts. Innovative Medicines vs. Generic Copy*, Rx&D website [www.canadapharma.org](http://www.canadapharma.org)). However, most industry observers who have not been paid by the brand-name pharmaceutical industry say these figures are grossly exaggerated.

### **Dr. Marcia Angell on Big Pharma's \$800-million per drug figure**

It was not until a year and a half later that the Tufts group actually published their analysis and it became possible to see how it was done. What they did was look at sixty-eight drugs developed at ten drug companies over about a decade. But the names of the companies and the names of the drugs were never revealed. Furthermore, all of the data on the costs of those drugs were supplied by the companies to the Tufts group confidentially, and as far as I can tell, the authors were not able to verify the information. They were supposed to take the companies' word, and we were supposed to take theirs. That situation is extremely unusual in scientific publishing, where it is understood that the salient data will be made available to readers so they can evaluate the analysis for themselves.

But one thing *is* clear from the paper. The \$802 million figure has nothing to do with the “average cost of developing a new drug,” in the words of *The New York Times*. It refers only to the cost of developing a tiny handful of the very most expensive drugs.

The Tufts analysis was restricted to new molecular entities (NMEs) developed entirely within the drug companies – what the authors called “self-originated NDEs” (the old term for NMEs). But these constitute only a tiny percentage of all new drugs.

There is a second problem with the Tufts estimate. It is not the actual out-of-pocket cost at all, even for the special group of drugs considered. That cost was \$403 million per drug. The \$802 million is what the authors call the “capitalized” cost – that is, it includes the estimated revenue that might have been generated if the money spent on R&D had instead been invested in the equity market.

And there is a third problem with the estimate. It is in pre-tax dollars. But R&D costs are fully tax deductible.

*The Truth About The Drug Companies: How They Deceive Us And What to Do About It*, Marcia Angell, M.D. Pages 42, 43, 44 & 45.

### Big Pharma breaking its R&D commitment to Canadians

The 2006 Annual Report of the Patented Medicine Prices Review Board (PMPRB) shows that for the sixth consecutive year Big Pharma's R&D-to-sales ratio has fallen below the level the industry promised when the Mulroney government passed Bill C-22.

**“With the adoption of the 1987 amendments to the Patent Act (Act), Canada's Research Based Pharmaceutical Companies made a public commitment that brand name manufacturers would increase their annual research-and-development (R&D) expenditure to 10% of sales revenue by 1996.”**

Patented Medicine Prices Review Board – Annual Report 2006, page 38

Pharmaceutical patentees spent only 8.1% of their revenues on research and development, below the 10% threshold the industry committed to in 1987.<sup>1</sup> It must also be noted that the 8.1% figure includes research expenditure funded by government grants. If the government-funded component is excluded, the R&D-to-sales ratio for pharmaceutical patentees in Canada drops to 7.9%.<sup>2</sup>

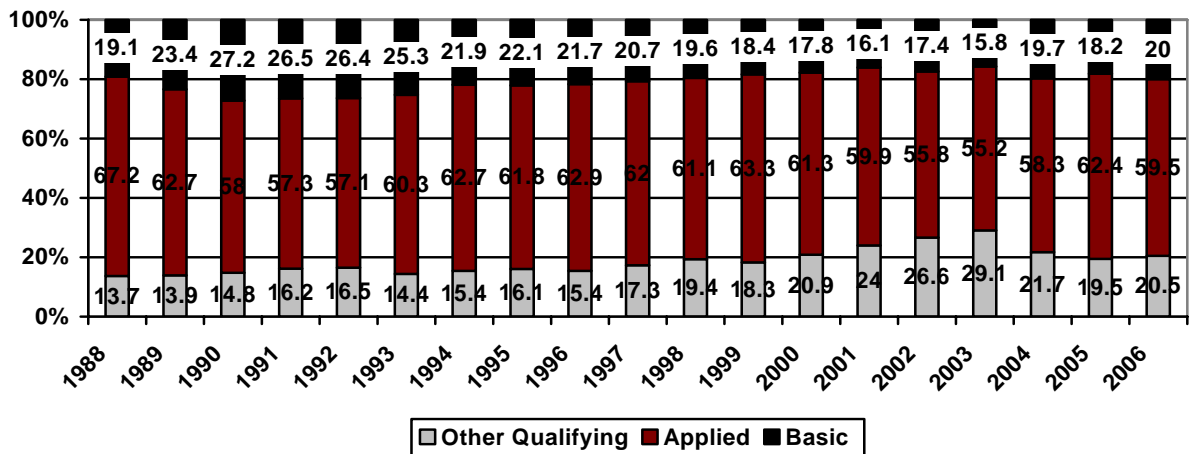
### Expenditure by type of research

Even more telling figures provided by the PMPRB are for allocation of research and development spending by type of research.

### Less than 2% of sales revenue spent on basis research

Patentees reported spending \$232.4 million on basic research, representing 20% of current R&D expenditure, or 1.9% of their Canadian sales revenue.<sup>3</sup>

**R&D Expenditure by Type of Research, 1988-2006<sup>4</sup>**



<sup>1</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 39

<sup>2</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 39

<sup>3</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 40

<sup>4</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 41

### Clinical trials account for nearly 80% of applied research

“Applied research is directed toward a specific practical application, comprising research intended to improve manufacturing processes, pre-clinical trials and clinical trials. Patentees reported spending \$689.6 million on applied research, representing 59.5% of current R&D expenditure. Clinical trials accounted for 77.3% of applied research expenditure.

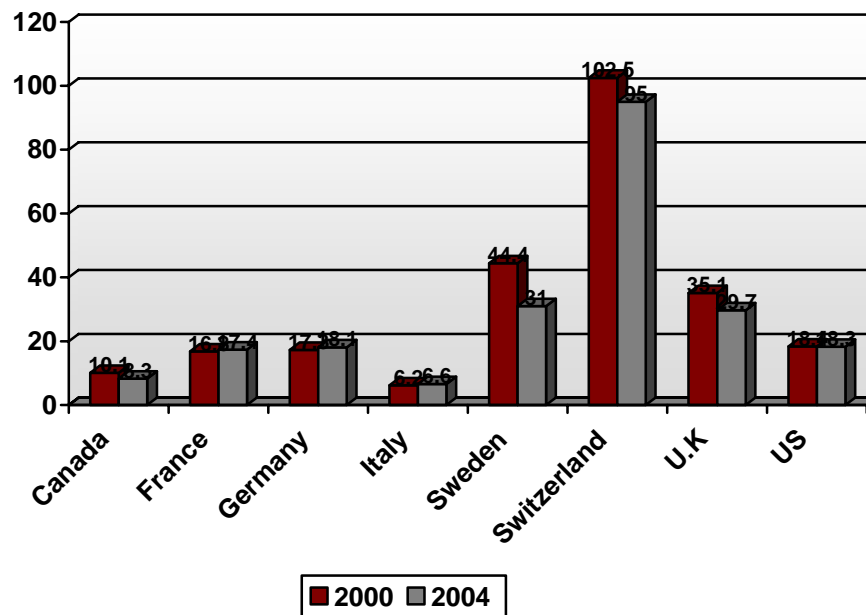
Other qualifying research (includes drug regulation submissions, bioavailability studies and Phase IV clinical trials) accounted for the remaining 20.5% of current expenditure in 2006.”<sup>5</sup>

### Canada’s pharmaceutical R&D spending well behind other countries

The PMPRB’s 2006 Annual Report also shows that the ratio of R&D to domestic sales in Canada remains well below values in the United States and Europe.

In 2000, the Canadian ratio was 10.1%. Only Italy (6.2%) had a lower ratio in that year. Switzerland had the highest ratio at 102.5%, followed by Sweden at 44.4%. France, Germany and the U.S. were in the 16 – 18% range, while the U.K. was more than double (35.1%). A very similar pattern emerges in the ratios for 2004. Italy (6.6%) remained at the bottom of the range, with Canada second lowest at 8.3%. Ratios in all other comparator countries were again well above Canada’s ratio.<sup>6</sup>

### R&D-to-domestic-sales ratios, Canada and 7 Comparator countries, 2000 and 2004<sup>7</sup>



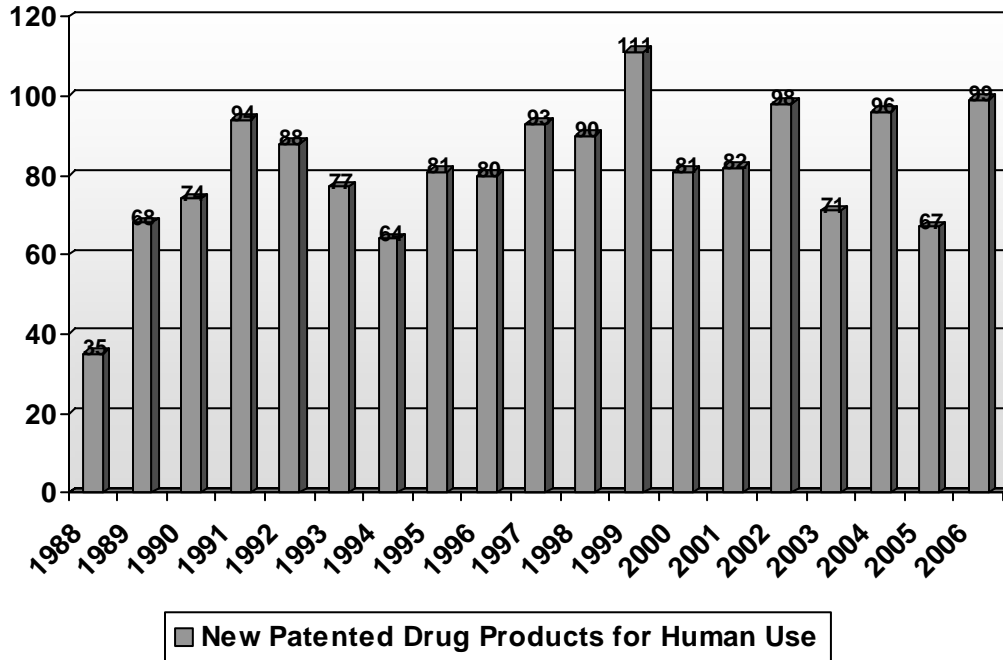
<sup>5</sup>Patented Medicine Prices Review Board – Annual Report 2006, page 41

<sup>6</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 43

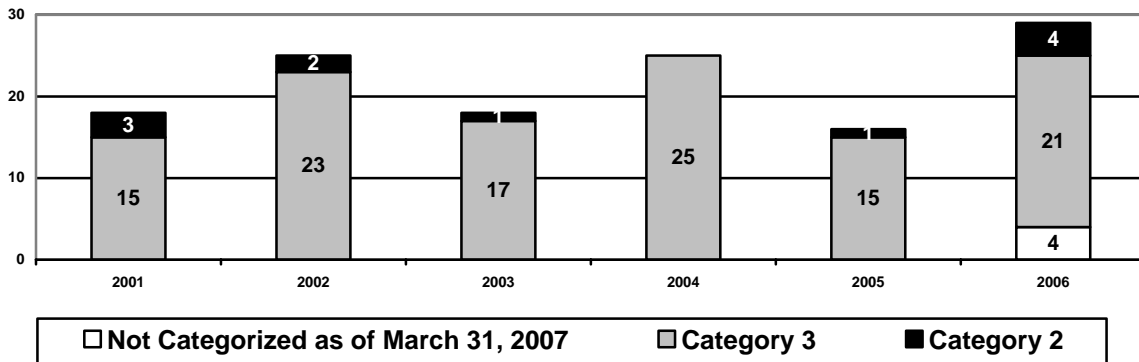
<sup>7</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 43

### Most “new” drugs not truly innovative

There were 99 new patented drug products, or DINs, for human use introduced in 2006. Some are one or more strengths of new active substances (NAS) and others are new presentations of existing medicines.<sup>8</sup>



In 2006, there were 29 new active substances. Of these, only 4 were Category 2, which the PMPRB defines as “the first drug to treat effectively a particular illness or which provides a substantial improvement over existing drugs products, often referred to as ‘breakthrough’ or ‘substantial improvement’”.<sup>9</sup> The vast majority (21 new active substances) were Category 3, which the PMPRB defines as “a new drug or new dosage form of an existing medicine that provides moderate, little or no improvement over existing medicines.” The remaining four new active substances were not categorized as of March 2007.



<sup>8</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 10

<sup>9</sup> Patented Medicine Prices Review Board – Annual Report 2006, page 12

## Taxol: A Case Study on Big Pharma's "Innovation"

Take the case of Taxol (the brand name for paclitaxel), the bestselling cancer drug in history. Now used to treat cancers of the ovary, breast and lung, it was derived from the bark of the Pacific yew tree in the 1960s. All of the research on the drug was conducted at, or supported by, the National Cancer Institute over nearly thirty years, at a cost to taxpayers of \$183 million. In 1991, Bristol-Myers Squibb signed a cooperative research and development agreement with the NCI – a deal made possible by the Stevenson-Wydler Act and a 1986 amendment called the Federal Technology Transfer Act. The company's part of the bargain was mainly to supply the NCI with seventeen kilograms of paclitaxel (which it obtained from a chemical company). No ingenuity there. In 1992, after Taxol was approved by the FDA for treatment of cancer of the ovary, entirely on the basis of NIH-supported research, Bristol-Myers Squibb was given five years of exclusive marketing rights.

The only remaining problem for Bristol-Myers Squibb was the fact the Pacific yew tree was in short supply. That problem was solved in 1994 by NIH-funded scientists at Florida State University. They devised a method to synthesize Taxol, which they promptly licensed to Bristol-Myers Squibb in return for royalties. No company ingenuity there, either.

The worldwide use of Taxol (for cancers of the ovary, breast, and lung) generated between \$1 and \$2 billion a year for Bristol-Myers Squibb and tens of millions in annual royalties for Florida State University. The company spent very little on R&D in getting initial FDA approval to treat cancer of the ovary, although it has undoubtedly spent substantial sums since then for testing the drug for other cancers. But that takes no ingenuity, either. The story of Taxol is a prime example of a taxpayer-supported research discovering a valuable and lucrative drug that was virtually given as a gift to a large drug company for marketing, commercial exploitation, and further development. The public pays again when it buys Taxol at the exorbitant price Bristol-Myers Squibb charges for a drug it neither discovered nor developed.

When it came on the market, Taxol sold for \$10,000 to \$20,000 for a year's treatment – reportedly a twentyfold markup over manufacturing costs. Bristol-Myers Squibb, you will recall, put next to nothing into the initial R&D, although it has since sponsored clinical trials aimed at expanding the uses of the drug. In a blazing act of hubris, the company fought tooth and nail to extend its exclusive rights on Taxol beyond the original five-year term, and managed to win another three years by suing the generic manufacturers who wanted to enter the market. As of 2003, the company had paid royalties to the NIH of only \$35 million on its \$9 billion in sales of Taxol (the agreement was 0.5 percent in royalties). Going in the other direction, the government paid Bristol-Myers Squibb hundreds of millions of dollars for Taxol through the Medicare program.

*The Truth About The Drug Companies*, Dr. Marcia Angell, pages 58, 66

**Increased patent protection has not resulted in increased R&D spending**

This data proves that 20 years of concessions to the brand-name pharmaceutical industry by the Government of Canada, including Bill C-22, Bill C-91 (which brought in the *Patented Medicines (Notice of Compliance) Regulations*) and Bill S-17, have had limited impact on research and development in Canada.

The vast majority of brand-name drug company R&D spending in Canada is to obtain regulatory approval so that their products can be marketed in Canada.

In terms of investment by brand-name companies in research and development, Canadians have received virtually nothing in return for these patent rules that they would not have already received solely due to the regulatory approval process for pharmaceutical products.

**Generic Pharmaceutical R&D Spending in Canada Outpaces Brands'**

The generic industry spends approximately \$450 million annually on research and development in Canada. In fact, one of CGPA's member companies, Toronto-based Apotex, is the largest R&D spender among all pharmaceutical companies in Canada – brand or generic.

According to Research Infosource's 2006 annual list of the top 100 corporate R&D spenders in Canada, Apotex spent \$183 million on R&D, which equals 18.3% of the company's sales. Number two on the list was brand-name giant Pfizer, which spent \$179 million on R&D, or 8.3% of its \$2.2 billion in Canadian sales.<sup>10</sup>

What is also significant about these figures is that generic pharmaceutical companies make these investments on sales of \$3.2 billion in Canada<sup>11</sup>. The remainder, or \$14.6 billion of the \$17.8-billion spent annually on prescription drugs in Canada, is spent on brand-name drugs<sup>12</sup>.

Even setting aside the significant savings that generic pharmaceuticals bring to Canada's health-care system, from a purely jobs and investment perspective, it is an indisputable fact that a dollar spent on a generic drug results in more jobs, more investment in R&D and more investment in pharmaceutical manufacturing capacity in Canada than a dollar spent on a brand-name drug.

---

<sup>10</sup> RESEARCH Infosource Inc. – Canada's Top 100 Corporate R&D Spenders 2006

<sup>11</sup> IMS Health Canada – 12 months ending December 2006

<sup>12</sup> IMS Health Canada – 12 months ending December 2006

## Pharmaceutical Industry Investment in Canada: Generic vs. Brand

### Canadian Sales

Total annual spending on prescription drugs:	\$17.8 billion
Brand name:	\$14.6 billion (81.9%)
Generic:	\$3.2 billion (18.1%)

### Total number of prescriptions filled

	410 million
Brand name:	228 million (55.5%)
Generic:	182 million (44.5%)

Source: IMS HEALTH - 12-months ending March 2006

### Employment in Canada

Brand name:	22,000 (Source: Rx&D)
Generic:	10,500

### Research and Development Spending in Canada

Brand name:	\$1.2 billion/8.1% of sales (Source: Patented Medicine Prices Review Board)
Generic:	\$450 million/15% of sales

## Canadian Trade Balances: Pharmaceutical and Medicine Manufacturing

Source: Statistics Canada, July 17, 2006

Value in Millions of Canadian Dollars

	1993	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005
Total Exports	516	684	816	940	1,327	1,562	1,681	1,853	2,307	2,552	3,401	4,011	4,335
Total Imports	2,072	2,360	2,643	2,927	3,298	4,196	5,086	5,962	7,044	8,055	8,993	9,507	9,986
Trade Balance	(1,556)	(1,666)	(1,827)	(1,987)	(1,971)	(2,634)	(3,405)	(4,109)	(4,737)	(5,504)	(5,592)	(5,496)	(5,651)

### Canada's Trade Deficit in Pharmaceutical and Medicine Manufacturing

As the chart above illustrates, data from Statistics Canada shows that Canada's trade deficit in pharmaceutical and medicine manufacturing has grown from \$1.6-billion in 1993 to \$5.7-billion in 2005.

Not only is Canada not getting its fair share of R&D spending from the brand-name pharmaceutical industry, this industry has restricted its manufacturing capacity in Canada thus leading to a flood of imports and only limited exports.

**Longer market monopolies through increased “data exclusivity”**

As the data above illustrates, despite the fact that the Government of Canada has increased market monopolies for brand-name drug companies several times over the past 20 years (C-22 in 1987, C-91 in 1992, S-17 in 2001), this has not resulted in more research and development spending in Canada as a percentage of sales. In fact, historical data from the PMPRB shows that the opposite is true.

Despite this evidence, in October 2006 the Government of Canada again increased monopoly rights for brand-name companies through regulatory amendments to “data exclusivity” provisions of the *Food and Drug Regulations*.

The October 5, 2006 amendments to the *Food and Drug Regulations* establish yet another regime to provide brand-name drug companies with an eight-and-one-half year (eight years plus six months pediatric exclusivity) ban on competition, even for non-patented drugs.

Under the new rules, a generic drug cannot receive Health Canada approval for eight years from approval of the equivalent brand-name drug, and the generic company cannot file its regulatory submission with Health Canada for at least six years after approval of the equivalent brand.

Canada’s pre-October 5, 2006 data protection regime of five years was in full accordance with international trade agreements such as the North American Free Trade Agreement (NAFTA) and the Trade-Related Aspects of Intellectual Property Right (TRIPS) agreement, and should have been left as it was.

The new regime goes far beyond provisions in the United States, and exceeds Canada’s trade commitments under NAFTA and TRIPS. Under data protection in the U.S., a generic drug submission cannot be filed for four years, and the generic is prevented from obtaining approval for only five years. Canada’s proposed eight years is 60 percent longer. Yet generic market penetration in Canada is much lower than in the US. In Canada 45 percent of prescriptions are filled by generic equivalents while that figure is 63 percent in the U.S., a gap that has widened in recent years. In fact, Canadians could save \$700-million on the cost of prescription medicines in the first year alone if the use of generic drugs increased to levels in the U.S.

This increased ban on competition will worsen the problem of soaring prescription drug costs in Canada. It is estimated that, had the eight-and-a-half-year ban on competition been in place over the past five years, it would have added at least \$600-million to prescription drug costs in Canada, more than \$100-million every year, and blocked Health Canada’s approval of lower-cost generic equivalents of block-buster medicines such as anti-depressants Zoloft and Wellbutrin and cholesterol reducer Pravachol.

**Six-month pediatric exclusivity**

An additional six months of market monopoly is granted to brand-name drug companies if they file clinical trials “designed and conducted for the purpose of increasing knowledge of the use” of the drug in pediatric populations “and this knowledge would thereby provide a health benefit in those populations”.

Under the new rules, eight years of data protection is extended to eight years and six months if pediatric trials are filed within five years of the brand-name product receiving its Health Canada approval.

The value of a six-month monopoly for a major drug could be tens of millions of dollars, far exceeding cost or value of a pediatric trial. The amendment will not encourage pediatric research, but will merely lengthen the brand-name drug companies’ market monopolies. Brand-name drug companies will merely submit the trials they have already done for the Food and Drug Administration (FDA) in the United States. Therefore the proposed amendment will not result in pediatric trials that would not otherwise be done.

**Conclusion**

From a public policy perspective, the most important and relevant question regarding the pharmaceutical patent regime is whether or not it is serving the interests of Canadians.

On the twentieth anniversary of the introduction of Bill C-22, which gave brand-name drug companies longer periods of market monopoly, and more than 14 years after the introduction of the *Patented Medicines (Notice of Compliance) Regulations* of Canada’s *Patent Act*, it is evident that the shift in Canada’s pharmaceutical policy in favour of brand-name drug companies has been a failure in virtually every measurable outcome.

It is clear that 20 years of concessions to the multi-national brand-name pharmaceutical industry by the Government of Canada has not served the interests of Canadians:

- Relative to other countries, increased pharmaceutical patent protection has not resulted in more research and development in Canada nor has it had any relation to the number of pharmaceutical products introduced in this country
- For six consecutive years, pharmaceutical patentees have failed to meet the minimum commitments for R&D spending in Canada that they made to the Canadian government when their state-sanctioned and enforced market monopolies were increased in 1987

- Historical data from the Patented Medicine Prices Review Board (PMPRB) shows the vast majority of brand-name drug company R&D spending in Canada is to obtain regulatory approval so that their products can be marketed in Canada. It is clear that increasing pharmaceutical patent protection in Canada has had limited impact on levels of research and development spending
- Of the 131 new active substances introduced in Canada from 2001 to 2006, only 11 were categorized by the PMPRB as a “breakthrough” or “substantial improvement” over existing drug products
- Given its enormous annual sales in Canada, brand industry job creation is quite low (22,000 jobs on \$14.8 billion in sales)
- Canada’s trade deficit in pharmaceutical and medicine manufacturing has increased from \$1.6 billion in 1995 to \$5.7 billion in 2005, which highlights the fact that the vast majority of brand-name drugs are not produced in Canada but shipped in from foreign countries
- Drug costs are the fastest rising cost in Canadian health care. Provincial governments are demanding changes as their drug benefit plan costs increase at annual rates of 10-15%.
- Drug benefits are increasingly becoming a major point of contention in labour negotiations as employers attempt to shift costs to employees