DISCUSSION AND DEBATE

Research Output of the Canadian Pharmaceutical Industry: Where Has All the R&D Gone?

Résultats de recherche dans l'industrie pharmaceutique canadienne : que sont devenus la recherche et le développement?

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Abstract

Although the Canadian pharmaceutical industry claims to be spending about $1 billion per year for research and development (R&D), there is little evidence of research performed, as measured by scientific publications and patent applications. One firm was exceptional; it compared favourably with its parent firm in regard to the number

of publications and patents in relation to the R&D budget, demonstrating the feasibility of developing a productive and independent research program in Canada. The perception of low productivity is made worse by the inadequacy of the annual report on R&D prepared by the Patented Medicines Prices Review Board (PMPRB). We recommend a number of changes in the PMPRB's mandate so that its collection of R&D data and subsequent analysis will be more complete. Further financial assistance to the industry should be withheld until accountability is assured and a full assessment of the outcome of its R&D program can be made.

Résumé

Bien que l'industrie pharmaceutique canadienne prétende consacrer environ un milliard de dollars par an à la recherche et au développement (R&D), il existe peu de preuves sur les travaux de recherche réalisés, à en juger par les publications scientifiques et les demandes de brevet. Une firme a eu des résultats exceptionnels : elle s'est en effet comparée favorablement à sa société mère pour ce qui est du nombre de publications et de brevets comparativement au budget de R&D, démontrant qu'il est possible d'élaborer un programme de recherche productif et indépendant. L'impression d'une faible productivité est renforcée par le rapport annuel lacunaire sur la R&D préparé par le Conseil d'examen du prix des médicaments brevetés (CEPMB). Nous recommandons d'apporter un certain nombre de changements au mandat du CEPMB afin de lui permettre de se livrer à une collecte et une analyse de données plus complètes en matière de R&D. On devrait placer un moratoire sur l'aide financière accordée à l'industrie jusqu'à ce qu'on puisse instaurer un système adéquat de reddition de comptes et procéder à une évaluation complète des résultats de son programme de R&D.

The pharmaceutical industry has consistently argued that the high cost of research and development (R&D) of new medications necessitates a long period of patent protection (R&D 2001; DiMasi et al. 2003). The government responded in 1987 by increasing market exclusivity to 7 or 10 years and total patent duration to 17 or 20 years (depending on the source country of the chemicals to be used) before compulsory licensing was permitted (Table 1). In exchange for the increased protection, brand-name manufacturers committed their firms to increase R&D activity so that the R&D/S (sales revenue) ratio would increase from 4.9% in 1987 to 10% in 1996 (Office of the Auditor General of Canada 1998: para. 17.11). Further, passage of Bill C-91 in 1992 stopped compulsory licensing completely, prohibited generic companies from stockpiling ingredients or products in preparation for release to market after the patent protection ended and established

the regulations concerning tax benefits for R&D. The current federal and provincial tax treatment and benefits associated with pharmaceutical R&D are more generous than those of any other nation (Warda 1999). There was a widely held conviction that these changes would result in an increase in the amount of basic pharmaceutical research done in Canada as well as an increase in jobs for degree-level scientists involved in that research (Côté 1986).

TABLE 1. Government Policy Changes

FAVOURING GENERIC FIRMS	FAVOURING BRAND-NAME FIRMS
1923:	**1987 Bill C-22:**
• Introduction of Compulsory Licensing	• 17 years of patent protection before compulsory licensing permitted
1969 Patent Act:	• 7 years of market exclusivity included
• Permitted importation of patented drug under compulsory license	**1993 Bill C-91:**
• Market exclusivity 7 years	• Compulsory licensing abolished
• Stockpiling ingredients to prepare for generic manufacturing	• 20 years of patent protection
	• Prohibited stockpiling ingredients to prepare for generic manufacturing
	• Evergreening*
	• Automatic Injunction**
	• Tax credit for R&D expenditure

*"Evergreening" is a term coined to describe the process of prolonging the period of market exclusivity by obtaining additional patents for what is essentially the same medication. The added patents may be for minor changes related to use (new dosage form or size), process of manufacturing or recognition of an active intermediate or active polymorphs and metabolites (Anderson 1997).
**New regulations (Bill C-91, passed in 1993) made approval by Health Canada to make and market a generic drug dependent on the patent status of the brand-name product with which it will compete; the generic maker must show that the patent has expired. If the patentee does not accept this claim, Health Canada is prohibited from approving the generic drug until both sides agree on the expiration, the dispute is settled in court or 24 months have elapsed. Since most settlements take at least 24 months, regardless of who is right, the process amounts to an automatic injunction against the generic firm (Anderson 1997).

Since both tax subsidies and patent protection are indirect expenses borne by society at large, it is reasonable for society to ask for an accounting of their costs and benefits. The purpose of this paper is to comment on the existing collaborations between the industry and the public sector with respect to both basic and applied research, our ability to measure research spending and productivity, and the actual levels of spending and productivity. The legislation referred to above defined the terms basic and applied research clearly and concisely: basic research is "work that advances knowledge without a specific application in view," while applied research is "that performed with

a specific practical application in view" (Consolidated Statutes and Regulations of Canada 1979; PMPRB 2005). In the context of the pharmaceutical industry, the goal of applied research is to bring a new product to market with market exclusivity protected by a patent, and applied research includes all the steps from laboratory work to Phase III clinical trials done with that new product in mind.

Background[1]

Closed science to open science

The past 50 years have seen radical changes in the way the pharmaceutical industry searches for new drugs. The traditional process consisted of screening a large number of randomly selected compounds against laboratory models of disease or of pathological processes, then purifying for further study any that seemed promising. This work was performed in-house and was highly confidential (closed science). In the current mode of drug development (knowledge-based drug design), knowledge that has been derived from all sources and is now in the public domain is used to develop hypotheses concerning the structure and properties of a drug that would be effective in a specific clinical state; such a drug can then be synthesized and tested. Knowledge-based drug design, being dependent on the availability of knowledge generated by the work of scientists in the public sector, fosters closer ties between scientists in industry and in the public sector, and is referred to as "open science" (Zucker and Darby 1996, 1997; Dasgupta and David 1944).

By increasing the use of knowledge from the public domain, an open science policy carries a major economic benefit to the industry; quantitative estimates indicate that the rate of return from basic research is on the order of 25% to 40% (Adams 1990; Griliches 1994). For private sector firms the degree of benefit is highly dependent on the "connectedness" of their scientists with those in the "upstream" academic science community (Cockburn and Henderson 1997). The industry understands the importance of the relationship: virtually all firms performing research in the life sciences have some type of working relationship with a university, and 25% of faculty members in the life sciences departments received financial support from the industry for their research (Blumenthal 2003). However, there may be a price for such support. First, the establishment by the Medical Research Council and the Canadian Institutes of Health Research of "partnerships" between industry and academia has given the pharmaceutical manufacturers an opportunity to influence the direction of public sector research with little financial responsibility. Second, the dependence of scientists

on research support from industry may lead some to bias their findings in favour of the drug firm (Bekelman et al. 2003). Finally, while one of the expected benefits of open science is greater communication among scientists, the development of close and exclusive academic-industrial ties may actually reduce communication.

Research spending

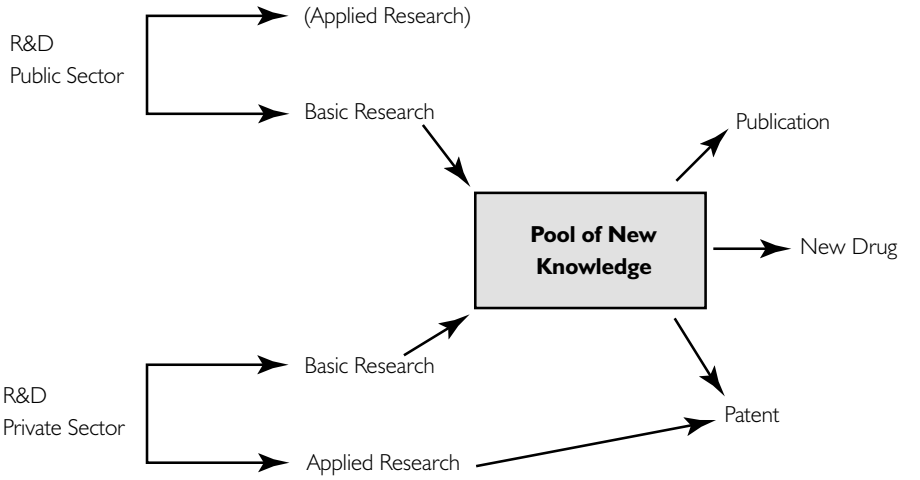
In response to Bill C-22, the member companies of the Pharmaceutical Manufacturers Association of Canada (PMAC; now named Rx&D) committed their firms to increase R&D expenditures as a percentage of sales to 10% by 1996 (Office of the Auditor General of Canada 1998: para. 17.11). The collection and reporting of information on R&D expenditures became the responsibility of the newly created Patented Medicines Prices Review Board (PMPRB). Although the 10% goal was achieved on time, the ratio has declined each year since. In 1999, spending in Canada was lower than in all countries in the G-7 except Italy (expressed as absolute amount, per capita amount, or percentage of domestic sales). Currently, it is well below the aggregate ratio for the smaller European countries too, although it does remain above its pre-1987 level (PMPRB 2002).

It must be noted that the above figures represent a best-case scenario because the PMPRB's analysis is limited. First, it receives information only on firms that sold patented medicines during a given calendar year. Second, the PMPRB does not have the authority to audit the figures submitted to it. Finally, there have been several mergers (Reger 2001; Tarabusi and Vickery 1998), particularly among the large firms, with centralization of small facilities (including Canadian subsidiaries) and loss of jobs. Consequently, determining the effect of Bills C-22 and C-91 on the creation and maintenance of research-related jobs has not been possible.

Measuring research output

Both basic and applied research lead to new knowledge, and the relationship between the two is shown in Figure 1. New knowledge obtained through basic research leads to publications, and new knowledge obtained through applied research leads to new drugs/methodologies and consequently new patents. Patent counts have been used frequently as indicators of output of R&D (OECD 1994; Hinloopen 2003; Adams and Griliches 1997). Further, patents are obtained to protect the ownership of the patented item. As there is no benefit to protecting an idea or observation that cannot contribute to drug development, all research leading to a patent application is, by definition, applied research. That being said, a measure using only patent information would underestimate total productivity because some applied research results may not help towards obtaining a patent but the results may still be worthy of publication.

FIGURE 1. Hypothesized relationships among research, the shared pool of scientific knowledge and applied research



Knowledge derived from basic research is available to all. When appropriate, new knowledge may be described in a scientific publication; occasionally, it may bring other information together and lead to a new drug or to a higher level of understanding that is patentable. The category "(Applied Research)" indicates that there is little research in the public sector that is undertaken with the purpose of developing a new medication.

Output of pharmaceutical research in Canada

We compared the major Canadian subsidiaries to their multinational parent firms regarding number of publications and number of patent applications, corrected for differences in R&D expenditures (Table 2) and the number of important new drugs marketed before and after Bill C-91 was passed (Table 3). Sources of information and details of methodology are given in the appendix to this paper. In brief, with the clear exception of Merck Frosst Canada, the subsidiaries had many fewer publications and patent applications per dollar of R&D, and there was no increase in the total number of new or Category 2[2] drugs per year after approval of Bill C-91. In contrast, the number of new drugs in the USA increased by 63% for the same period (Hunt 2002).

Discussion

Prior to Bill C-22, there was a widespread view that the low level of R&D spending in Canada was a response to our "hostility" towards the pharmaceutical industry. Although the Canadian tax treatment of R&D is now more generous than that of any other nation (Warda 1999), there has been no increase in the production of basic research, in the rate of introduction of new drugs or in the relative number of

TABLE 2. Publications and patent applications of parent firms and Canadian subsidiaries (1998–2004)

PARENT	R&D[1]	PUB[2]	PAT[3]	(PAT+PUB)/(R&D)
ABBOTT	10,284	2,996	733	0.36
ASTRAZENECA	18,102	3,433	790	0.23
AVENTIS PHARMA	19,884	2,623	1096	0.19
BRISTOL-MYERS SQUIBB	14,356	2,399	610	0.21
JOHNSON & JOHNSON	25,814	1,043	496	0.06
MERCK	18,554	7,282	1500	0.47
NOVARTIS PHARMA	25,652	5,420	760	0.24
PFIZER	36,614	4,516	835	0.15
WYETH	12,862	2,060	421	0.19
SUBSIDIARY	**R&D[1]**	**PUB[2]**	**PAT[3]**	**(PAT+PUB)/(R&D)**
ABBOTT LABORATORIES	63	0	0	0
ASTRAZENECA CANADA	506	18	1	0.04
AVENTIS PHARMA	267	2	0	0.01
BRISTOL-MYERS SQUIBB CANADA	316	2	0	0.01
JOHNSON & JOHNSON MERCK	0	0	0	0
MERCK FROSST CANADA	690	194	211	0.59
NOVARTIS PHARMA CANADA	334	6	0	0.02
PFIZER CANADA	815	24	0	0.03
WYETH AYERST CANADA	277	0	0	0

1 Research and development expenditure ($000s)
2 Publications in scientific and professional journals
3 Number of patents applied for

TABLE 3. New drugs marketed since patent law enacted

	CATEGORY 2 / PRIORITY NME*		OTHER	
	1989–1994	1995–2000	1989–1994	1995–2000
Canada	36	26	477	521
USA	73	80	277	489

*Category 2 for Canada; Priority NME for US

Category 2 drugs. Because the Canadian pharmaceutical industry is again lobbying for more patent protection, less stringent price controls and better tax treatment for R&D expenditure as methods to promote R&D and make Canada a leader in drug development (Rx&D 2004), we believe it is important to understand why the previous legislation did not achieve its objectives.

With respect to basic research productivity, it is possible that we omitted basic research undertaken extramurally and credited to other organizations (e.g., hospitals and universities). However, the results of basic research have no immediate commercial value, need not remain confidential and thus would be publishable in the public domain. Further, authors are required to acknowledge the sponsoring company in the publication. We therefore believe it unlikely that we missed more than the occasional title. Although many pharmaceutical manufacturers engage other private companies to perform Phase I trials and targeted drug development, this is applied research by definition. Finally, because we are comparing Canadian and parent companies, any omission due to our methodology would affect the conclusions of the analysis only if it applied solely to the Canadian company or the parent company but not both; we believe this is unlikely.

With respect to applied research, one possible reason for the parent–subsidiary difference is that the development of new drugs targeted to the Canadian population may not be economical; an OECD study (Burstall et al. 1981) and the Eastman report (Commission of Inquiry on the Pharmaceutical Industry 1985) emphasized the small size of the Canadian market, the high cost of an independent research establishment and the efficiency of obtaining information and technology from established programs. Parent firms with only a minimal intramural research program in Canada may therefore have decided, as a matter of policy, that any promising development originating from these small operations would be transferred to the parent research centre. However, the experience of Merck Frosst Canada Research Institute provides clear evidence of the feasibility of creating a Canadian research enterprise under current conditions, and the success of Premarin and Vioxx demonstrates that a drug developed in Canada may have access to the same broad market as that available to the parent firm. Finally, regardless of the reason, failure to observe a time-dependent increase in research output suggests that increased patent protection and tax credits did not accomplish the stated goals, and "more of the same" (Rx&D 2004) is unlikely to produce a better result.

Limitations of the analysis

It was not possible to analyze the basic and applied research spending separately by location (intramural, hospitals and universities, other companies). The PMPRB reports provide only aggregate spending by type of research (basic or applied) or by

location (Tables 15/16 in the 2004 report), but not both. We are also concerned with the PMPRB's classification of basic and applied research. Table 15 of its 2004 report appears to classify all production process or pre-clinical/clinical trials as applied research, and all laboratory-based research as basic science. This classification is incompatible with the currently recognized definitions described above. For any division of R&D into "basic" and "applied" research to be valid, these terms must be used consistently and accurately. These problems would be solved if the list of projects and resulting publications supported by the pharmaceutical firms is made public. Finally, all figures are based on what is provided by the industry because the PMPRB does not have the authority to verify the reported R&D expenditures. This is an obvious concern in the evaluation of a government program designed to meet specific targets.

The Auditor General has also noted that the PMPRB was established under the Patent Act (1992), while the R&D expenditures eligible for tax benefits are those that would have been eligible under the income tax legislation in effect on December 1, 1987. Because income tax regulations have changed several times since 1992 (new legislation is applicable to all non-pharmaceutical industries), the tax credit for R&D in the pharmaceutical industry is now unclear (Office of the Auditor General of Canada 1998: para. 17.67–17.69). This problem could be avoided by placing the pharmaceutical R&D tax expense regulations within the Income Tax Act, as is currently the case for all other industries.

Recommendations

Traditionally, government subsidies and tax initiatives are used to help industries that are considered strategically important in the overall national economy and that are in temporary financial difficulty. Although the pharmaceutical industry itself is expected to argue forcefully for every advantage, Canadians must decide whether continuing to subsidize the pharmaceutical industry at the expense of other parts of the economy is in their best interest. Should government increase the profits of an already profitable endeavour? How should we rate the importance of an industry when the large majority of its new products offer little or no advantage over those already available (Table 3)? If other industrialized countries provide subsidies, how "competitive" are we willing to be to induce the large firms to locate in our jurisdiction? To make these decisions, we must have valid and adequate data on the present situation; and if we decide to continue to subsidize this industry, we must be assured of obtaining unambiguous data to determine whether legislative objectives are being met. We recommend that the following steps be taken to ensure the availability of such information:

1. All pharmaceutical manufacturers that submit claims for tax credits for R&D to Revenue Canada must provide information to the PMPRB (current legislation

requires only Rx&D members to do so).
2. The PMPRB must have the authority and the budget to verify the claims submitted.
3. Each firm must provide the PMPRB with the amount of support for (a) each basic research project (non-confidential, by definition) and the publications resulting from them and (b) each applied research project that results in publication or patent applications. The list of projects should be divided into subgroups by research location (intramural, hospitals and universities, other companies) to allow an assessment of the quantity and quality of the research done by each group.
4. The tax laws pertaining to the research expenditures of the pharmaceutical industry should follow the tax laws of all other industries.

Summary

After initially raising R&D spending to a previously determined level, the Canadian pharmaceutical industry has steadily lowered its expenditure. Further, based on available data, longer patent protection and increased R&D spending do not appear to have increased research productivity. The industry is again requesting increased tax breaks and extended patent protection. We believe that continuation of present tax and patent support and any future benefits should be considered only when a proper system of accountability is available.

NOTES

1. This background information is based on Gambardella 1995 and Cockburn and Henderson 1997.

2. A Category 2 drug is one that is the first to treat effectively a particular illness or that provides a substantial improvement over existing drug products; often referred to as a "breakthrough" drug.

Appendix

Methods and results

Canadian subsidiaries were compared to their parent companies with regard to the number and category of new drugs marketed, the number of patents and scientific publications and the expenditure on R&D.

Number and category of new drugs

Hunt (2002) examined the level of innovation of new drugs approved by the FDA in

the period 1989–2000 using the categories shown in Table 4. To determine whether there was a change during that period he compared the data for 1989–1994 with those for 1995–2000. We compared the drugs approved by the PMPRB with the US results for the same periods. In the United States, there was a 63% increase in the number of new drugs marketed in the second period; all were of "ordinary" priority. In Canada, there was no significant change in either the total number of new drugs or in Category 2 drugs (Table 3).

TABLE 4. Classification of approved drugs

UNITED STATES (FDA)	CANADA (PMPRB)
New Molecular Entity Drug whose active ingredient has never before been approved by the FDA for the US market	**New Active Substance**
Incrementally Modified Drug Medicine that relies on an active ingredient present in a drug already approved (or a closely related chemical derivative), and has been modified by the manufacturer	**Category 2** The first drug to treat effectively a particular illness, or which provides a substantial improvement over existing drug products
Other Drug Drug using an active ingredient that is already available in an identical marketed product	**Category 3** A new drug or new dosage form of an existing medicine that provides moderate, little or no improvement over existing medicines
Priority Drug A product qualifying for the FDA's fast "priority review" because it appears to offer clinical improvement over available products and therapies in efficacy, safety, compliance, or use in a new sub-population	**Category 1** A new DIN of an existing or comparable dosage form off an existing medicine, usually a new strength of an existing drug
Standard Drug A product that does not qualify for "priority review" because it does not demonstrate significant improvement over marketed products	

Number of scientific publications and of patent applications

This and the following comparison were limited to the firms that were most consistently among the 10 largest with regard to sales in the US market, and that published

an annual report for the US corporation or for the US component of a European corporation. For each firm, we obtained the number of publications in which the institutional affiliation (as a search term) of one or more authors was the pharmaceutical firm of interest. Using this search strategy, we did a simultaneous search of the databases Current Contents, Embase and Medline, then eliminated the duplications to get a corrected total. Using annual sales figures provided by IMS Health and R&D/S ratios as reported by PMPRB, we calculated the R&D expenditures of the Canadian subsidiaries; expenditures of the parent firms were taken from their annual reports. The number of patent applications for the period 1998–2004 was obtained by searches of the Canadian Patents Database of the Canadian Intellectual Property Office, using keyword searches in the advanced search option. The searches were performed with the name of the firm in the "owner" field. Total values for publications, patent applications and R&D expenditures for the period 1998–2004 are shown in Table 2. An approximation of research efficiency is given by the ratio of the sum of publications and patents (units of output) to R&D expenditure. Only the Merck subsidiary had a ratio of the same magnitude as the parent firm; the others had ratios 1/20th to one-fifth as large as the parent ratios.

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REFERENCES

Adams, J.D. 1990. "Fundamental Stocks of Knowledge and Productivity Growth." *Journal of Political Economy* 98(4): 673–702.

Adams, J. and Z. Griliches. 1997. *Measuring Science: An Exploration.* NBER Working Papers No. 5478. Vancouver: National Bureau of Economic Research.

Anderson, M. 1997. *Evergreening in the Canadian Pharmaceutical Industry.* Kingston, ON: Centre for Health Policy, Queen's University.

Bekelman, J.E., Y. Li and P. Gross. 2003. "Scope and Impact of Financial Conflicts of Interest in Biomedical Research: A Systematic Review." *Journal of the American Medical Association* 289(4): 454–65.

Blumenthal, D. 2003. "Academic–Industrial Relationships in the Life Sciences." *New England Journal of Medicine* 349(25): 2452–59.

Burstall, M.L., J.H. Dinning and A. Lake. 1981. Multinational Enterprises, Governments and Technology – The Pharmaceutical Industry. Paris: OECD. As quoted in J. Lexchin, 1993,

"Pharmaceuticals, Patents and Politics: Canada and Bill C-22." *International Journal of Health Services* 23: 147–60.

Cockburn, I. and R. Henderson. 1997. *Public–Private Interaction and the Productivity of Pharmaceutical Research.* NBER Working Papers No. 6018. Vancouver: National Bureau of Economic Research.

Commission of Inquiry on the Pharmaceutical Industry. 1985. Report of the Commission. Ottawa: Supply and Services Canada. As quoted in J. Lexchin, 1993, "Pharmaceuticals, Patents and Politics: Canada and Bill C-22." *International Journal of Health Services* 23: 147–60.

Consolidated Statutes and Regulations of Canada. 1979. *Income Tax Regulations.* Part XXIX, Scientific Research and Experimental Development, para. 2900 (1) (a)–(b).

Côté, M. 1986 (June 27). Notes for remarks by the Hon. Michel Côté, Minister of Consumer and Corporate Affairs.

Dasgupta, P. and P. David. 1944. "Towards a New Economics of Science." *Research Policy* 23: 487–521.

DiMasi, J.A., R.W. Hansen and H.G. Grabowski. 2003. "The Price of Innovation: New Estimates of Drug Development Costs." *Journal of Health Economics* 22: 151–85.

Gambardella, A. 1995. *Science and Innovation: The US Pharmaceutical Industry During the 1980s* (pp. xvi, 199). Cambridge, New York and Melbourne: Cambridge University Press.

Griliches, Z. 1994. "Productivity, R&D and the Data Constraint." *American Economic Review* 84(1): 1–23.

Hinloopen, J. 2003. "Innovation Performance across Europe." *Economic Innovation and New Technology* 12(2): 145–61.

Hunt, M. 2002. *Changing Patterns of Pharmaceutical Innovation.* Washington, DC: Research and Educational Foundation, National Institute for Health Care Management.

Office of the Auditor General of Canada. 1998. "The Patented Medicines Prices Review Board." *Report of the Auditor General* (Chapter 17, para. 17.11; para. 17.67–17.69). Ottawa: Author.

Organization for Economic Cooperation and Development (OECD). 1994. "Using Patent Data as Technology Indicators." In *Patent Manual.* Paris: Author.

Patented Medicines Prices Review Board (PMPRB). 2002. *A Comparison of Pharmaceutical Research and Development Spending in Canada and Selected Countries.* PMPRB Study Series S-2017. Ottawa: Author.

Patented Medicines Prices Review Board (PMPRB). 2005. *Annual Report 2004* (Glossary: 41). Ottawa: Author.

Rx&D. 2001. *The Development of an Innovative Medicine.* Ottawa: Author.

Rx&D. 2004. *Towards Increasing Research and Development in Canada: A New Innovative Pharmaceutical Strategy.* Ottawa: Author.

Reger, G. 2001. "Internationalization of Research and Development in Pharmaceuticals." In A. Jungmittag, G. Reger and T.H. Reiss, eds., *Changing Innovation in the Pharmaceutical Industry.* Berlin: Springer.

Tarabusi, C.C. and G. Vickery. 1998. "Globalization in the Pharmaceutical Industry, Part II." *International Journal of Health Services* 28(2): 281–303.

Warda, J. 1999. *Rating R&D Tax Incentives*. Members' Briefing 277-99. Ottawa: The Conference Board of Canada.

Zucker, L.G. and M.R. Darby. 1996. "Star Scientists and Institutional Transformation – Patterns of Invention and Innovation in the Transformation of the Biotechnology Industry." *Proceedings of the National Academy of Science* 93(23): 12709–16.

Zucker, L.G. and M.R. Darby. 1997. "Present at the Biotechnological Revolution – Transformation of Technological Identity for a Large Incumbent Pharmaceutical Firm." *Research Policy* 26(4–5): 429–46.

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