

The Pharmaceutical Industry and the Canadian Government: *Folie à Deux*

L'industrie pharmaceutique et le gouvernement canadien : folie à deux



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Abstract

The interest of the pharmaceutical industry is in achieving a profit for its shareholders while the interest of the Canadian government should be in protecting public health. However, over the course of the past few decades the actions of the Canadian government have been tilted in favour of industry in two areas. The first is in the relationship between industry and Health Canada and is manifested in the regulation of clinical trials, the drug approval system, drug safety and promotion. The second is in economic policy as it applies to policies about patent protection, the price of medications and measures taken to incentivize research and development. The problems in the relationship are structural and will only be solved through systemic changes.

Résumé

L'intérêt de l'industrie pharmaceutique est d'obtenir du profit pour ses actionnaires, tandis que l'intérêt pour le gouvernement canadien devrait être de protéger le public. Toutefois, au cours des dernières décennies, les actions du gouvernement canadien ont penché en faveur de l'industrie dans deux domaines. Le premier a trait à la relation entre l'industrie et Santé

Canada et se manifeste dans la réglementation des essais cliniques, le système d'approbation, la sécurité et la promotion des médicaments. Le deuxième touche à la politique économique dans le secteur de la protection conférée par les brevets, aux prix des médicaments et aux mesures prises pour encourager la recherche et le développement. Les problèmes de la relation sont d'ordre structurel et ne se résoudront que par des changements systémiques.

Introduction

As a doctor working in an emergency department, I write prescriptions every time I work, and I believe that these prescriptions help my patients. I have great respect for the value of medications when they are affordable and used properly. However, at the same time, I believe that government and industry have come to share far too many of the same goals in two areas – the drug regulatory system and industrial policy as it relates to intellectual property rights (IPRs), research incentives, drug prices and views about innovation. These are issues that I will explore primarily in the Canadian context, although occasionally drawing on American data. While the details in this article are Canadian, the issues faced are common to pharmaceutical policy in most of the developed world.

Profits versus Public Health

A number of systemic problems have led to our current situation. I start from the position that we should not be under any illusion about why pharmaceutical companies exist. Like any other corporations, they have an obligation to make profits for shareholders and investors. They should, therefore, do whatever is legal to advance this objective. However, the companies' economic aims often seem to conflict with their declared goal of improving health. As Davis and Abraham point out (Davis and Abraham 2013), society has a dual expectation from the pharmaceutical industry. On the one hand, companies should make profits for shareholders and investors, while on the other, the products that they produce should also provide a health benefit. From the viewpoint of the industry, that is exactly what it has been doing, and its economic success is a mirror of the success that it has had in creating products and innovations needed by patients. Governments also recognize the dual nature of the industry and "have not been so naive as to accept that the pharmaceutical industry's commercial motives will always deliver new drug products in the best interests of patients" (Davis and Abraham 2013). As a result, government drug regulatory agencies exercise a check on drug companies' claims both before and after products are marketed. However, governments face conflicting objectives. On the one hand, they recognize the need to regulate the industry in the interests of public health, but on the other hand they also rely on the industry to help fuel their economies. The question that I want to pose is, whose interests are being served in the way that the state is regulating the industry?

Neo-liberalism and Deregulation

My answer is that, with a few exceptions, most western states have sought cooperation with the pharmaceutical industry. The alliance of interests between the state and the industry has not been static but has markedly increased over the past two decades as the neo-liberal agenda gained momentum in the mid-1980s, accelerating the deregulatory trend and further deepening the relationship between the two. Neo-liberalism is focused on the power of the marketplace and supports a diminished role for the state in protecting its citizens by letting industry set its own regulatory standards and police them. This acceleration in the deference to industry is best understood in the context of corporate bias. The state did not completely surrender its regulatory role, but attempts to exert more authority were undertaken in a half-hearted manner that avoided confrontation with industry and actually strengthened the position of industry. As one example, we only need to look at the regulation of post-marketing studies in Canada. Post-marketing studies are of particular importance with respect to drug safety, given that even relatively large efficacy trials have insufficient power to detect rare but serious adverse events. Despite these limitations, fulfillment of the requirement to undertake these studies and complete them in a timely manner is poorly enforced in both Canada and the US (Fain et al. 2013; Law 2014) leading to a situation whereby the true benefits and harms of drugs remain unknown for years.

Often, government has gone beyond cooperation and actively promoted industry's interests through legislation and policies, even when industry's interests conflicted with those of the public, as is the case with the adoption of user fees whereby the pharmaceutical industry funds some or all of the operating costs of the regulatory authority. As the head of the drugs program branch of Health Canada put it in an internal 1997 bulletin that discussed user fees: "the client is the direct recipient of your services. In many cases this is the person or company who pays for the service." The one-page document focused on service to industry and relegated the public to the secondary status of "stakeholder" or "beneficiary" (Michols 1997). Regulatory authorities took on the obligation of meeting the needs of their clients, especially when it came to how quickly drugs went through the regulatory review process. Each day of delay in getting a drug onto the market could mean the loss of millions of dollars in sales. With speedier drug reviews now a priority, regulatory authorities devised new pathways to get drugs through the system at a faster rate (Darrow et al. 2014) with lower standards of evidence (Kesselheim et al. 2015) and a higher level of safety problems once drugs appear on the market (Carpenter et al. 2008; Lexchin 2012b, 2014; Olson 2002).

In other areas such as promotion most governments have voluntarily turned over *de facto* regulatory power to industry (Lexchin 2012a; Lexchin and Mintzes 2014) with the result that when doctors get their prescribing information directly from pharmaceutical companies the outcome is highly likely to be more expensive prescribing, more frequent prescribing and poorer quality of prescribing (Spurling et al. 2010).

Neo-liberalism fitted well with government's smart regulatory agenda, a move to decrease the regulatory burden on companies, and with the belief that providing the conditions for industry investment and research and development (R&D) would inevitably produce better drugs, better health, more economic activity, and more high-end jobs in the knowledge economy. This attitude was exemplified in a Canadian government document touting smart regulation as a way to put the emphasis on removing barriers and so move Health Canada to a place where it could "regulate in a way that enhances the climate for investment and trust in the markets [and] ... accelerate reforms in key areas to promote health and sustainability, to contribute to innovation and economic growth, and to reduce the administrative burden on business" (Government of Canada 2002).

The key, according to government thinking, was to make sure that companies could retain monopoly rights to the medications for long enough to generate the profits necessary to produce the next generation of "wonder" drugs. And, of course, respect for IPRs as private property was a necessary component of this equation.

Stronger Intellectual Property Rights

When it comes to economic and industrial policy, the best interests of the pharmaceutical companies do not necessarily coincide with what is best for the entire country and for public health writ large. Here again, we assume that government should balance these interests when it makes decisions about IPRs, how much drugs should cost and how best to encourage research that advances public health. Thus, in Canada, federal governments from the right (Conservative) and centre (Liberal) were willing to cooperate with industry demands for longer and more stringent patent rights and to put in place regulations to delay the entry of generic products (Lexchin 2011).

On the economic front, better IPR protection certainly benefits industry, but it is hard to demonstrate that it has helped the overall Canadian economy or the health of Canadians. However, it has generated costs in the form of legal expenses, longer monopoly periods with higher prices, vast sums spent researching and developing "me too" drugs that constitute almost 90% of products approved (Light et al. 2013), billions of dollars spent on drug promotion and restriction on the dissemination of research results to maintain a commercial advantage (Baker and Chatani 2002). Up until the mid-1980s, Canada relied on a system of compulsory licensing to import to keep drug prices in check. The decision to ratchet up IPRs and abolish compulsory licensing is one of the reasons that Canada now has the fourth highest annual per capita spending on prescription drugs in the Organisation for Economic Co-operation and Development (OECD 2015). Companies do not price products based on their R&D costs but rather on what they think that the market will bear, an interpretation endorsed by senior drug company executives (McKinnell 2005). The more desperate the patients are for the drug, the higher the price. This is painfully evident in the prices in Canada of Kalydeco (ivacaftor) for cystic fibrosis and Soliris (eculizumab) for atypical hemolytic uremic syndrome at \$300,000 and \$700,000 per year per person, respectively.

Who Benefits from Industry Research and Development?

Policy decisions about R&D have been predicated on the assumption that more R&D is better and that stronger IPRs are necessary to achieve the desired R&D spending. Industry has often encouraged that attitude with both threats of withdrawing R&D investment and promises of increasing investment, all contingent on the amount of IPR protection that is offered. But even senior pharmaceutical executives discount the importance of the strength of IPRs in making decisions about where to locate R&D. Instead, they cite a location in which they could do good science by accessing world-leading scientists as the most important factor. The only time that IPRs figured into their thinking was when it came to countries such as India and China that were perceived as having inadequate systems for protecting IPRs (Bramley-Harker et al. 2007).

Governments have also failed to recognize the difference between the industry definition of innovation as a new molecule and the patient-oriented definition as a drug that substantially improves health. New molecules can be spectacularly profitable as witnessed by Lipitor (atorvastatin) that made Pfizer \$125 billion over 14.5 years (’t Hoen 2016) but that does not necessarily mean that they are better than alternatives for patients. On the latter measure, industry R&D outputs leave a lot to be desired. Between 1997 and 2012, Health Canada approved 292 new active substances (molecules never marketed before in any form) where both their therapeutic value and mechanism of action could be evaluated. Ninety-eight were first-in-class, i.e., operated through a novel mechanism, but only 16 (16.3%) of these were significant therapeutic advances. For the remaining 194, the situation was even worse with just 9 (4.6%) rated as a significant therapeutic advance (Lexchin 2016). Cancer drugs fare no better. The 71 drugs approved by the US Food and Drug Administration from 2002 to 2014 for solid tumours have resulted in median gains in progression-free and overall survival of only 2.5 and 2.1 months, respectively (Fojo et al. 2014)

How to Make Government Serve the Public Interest

The problems we are seeing are, obviously, not the result of individuals working within the drug companies or the government. In fact, many good people work in all sectors. The problems are structural and only systemic changes will help solve them. However, despite both parties – government and industry – being part of the problem, only one, government, is part of the solution. To quote Davis and Abraham, “the narrowly construed definition of regulatory efficiency as speed of regulatory review and marketing approval during the neo-liberal era has been misguided from the perspective of the interests of patients and public health, though it has served the commercial interests of industry” (Davis and Abraham 2013). Regulatory authorities’ primary purpose is the protection of public health, and as such, they should be entirely publicly funded so that there is no confusion about who their client is. In the US, this recommendation has come from a variety of high profile academics and others including three former editors of the *New England Journal of Medicine* and former senior employees of the Food and Drug Administration (Angell et al. 2007). Fetishization of IPRs

is good for the economic health of industry but not for the results of R&D or drug prices. Canada, in cooperation with other countries, should actively advocate for alternatives to the patent system for supporting pharmaceutical innovation and fund pilot projects to look at the feasibility of alternative models. These could include public funding of clinical trials (Baker 2008; Lewis et al. 2007) and paying companies a monetary reward that reflects the social value of new medications in return for the companies surrendering their monopoly patent rights (Grootendorst 2009). Governments need to put more weight on protecting public health and reducing wasteful spending on drugs with no therapeutic advantages over existing products, and less on protecting the interests of the pharmaceutical industry. Doing so will benefit both patients and the public purse.

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References

- Angell, M., J. Avorn, E. Bingham, D. Carpenter, R. Alta Charo, R. Crout et al. 2007. "An Open Letter to: Chairman Edward Kennedy and Senator Mike Enzi, Chairman John Dingell and Representative Joe Barton, Members of the Senate Health, Education, Labor and Pensions Committee, Members of House Energy and Commerce Committee." Retrieved June 19, 2017. <[https://www.pharmamedtechbi.com/~media/Images/Publications/Archive/The Pink Sheet/69/016/006901600007/pdufa_open_letter.pdf](https://www.pharmamedtechbi.com/~media/Images/Publications/Archive/The%20Pink%20Sheet/69/016/006901600007/pdufa_open_letter.pdf)>.
- Baker, D. 2008. "The Benefits and Savings from Publicly Funded Clinical Trials of Prescription Drugs." *International journal of Health Services* 38: 731–50.
- Baker, D. and N. Chatani. 2002. *Promoting Good Ideas on Drugs: Are Patents the Best Way? The Relative Efficiency of Patent and Public Support for Bio-Medical Research*. Washington, DC: Center for Economic and Policy Research.
- Bramley-Harker, E., D. Lewis, J. Farahnik and R. Rozek. 2007. *Key Factors in Attracting Internationally Mobile Investments by the Research-Based Pharmaceutical Industry*. London, UK: NERA Economic Consulting.
- Carpenter, D., E.J. Zucker and J. Avorn. 2008. "Drug-Review Deadlines and Safety Problems." *New England Journal of Medicine* 358: 1354–61.
- Darrow, J., J. Avorn and A. Kesselheim. 2014. "New FDA Breakthrough-Drug Category – Implications for Patients." *New England Journal of Medicine* 370: 1252–58.
- Davis, C. and J. Abraham. 2013. *Unhealthy Pharmaceutical Regulation: Innovation, Politics and Promissory Science*. Houndmills, Basingstoke, Hampshire and New York, NY: Palgrave Macmillan.
- Fain, K., M. Daubresse and G. Alexander. 2013. "The Food and Drug Administration Amendments Act and Postmarketing Commitments." *JAMA* 310: 202–04.
- Fojo, T., S. Mailankody and A. Lo. 2014. "Unintended Consequences of Expensive Cancer Therapeutics – The Pursuit of Marginal Indications and a Me-Too Mentality That Stifles Innovation and Creativity. The John Conley Lecture." *JAMA Otolaryngology Head and Neck Surgery* 140: 1225–36.
- Government of Canada. 2002. "The Canada We Want: Speech from the Throne to Open the Second Session of the Thirty-Seventh Parliament of Canada." Retrieved February 15, 2004. <www.pco-bcp.gc.ca/sft-ddt/docs/sft2002>.
- Grootendorst, P. 2009. "How Should We Support Pharmaceutical Innovation?" *Expert Review of Pharmacoeconomics & Outcomes Research* 9: 313–20.
- Kesselheim, A., B. Wang, J. FrankLin and J. Darrow. 2015. "Trends in Utilization of FDA Expedited Drug Development and Approval Programs, 1987–2014: Cohort Study." *BMJ* 351: h4633.

- Law, M. 2014. "The Characteristics and Fulfillment of Conditional Prescription Drug Approvals in Canada." *Health Policy* 116: 154–61.
- Lewis, T., J. Reichman and A. So. 2007. "The Case for Public Funding and Public Oversight of Clinical Trials." *Economists' Voice* 4(1): 1–4.
- Lexchin, J. 2011. "Canada's Patented Medicine Notice of Compliance Regulations: Balancing the Scales or Tipping Them?" *BMC Health Services Research* 11: 64.
- Lexchin, J. 2012a. "Models for Financing the Regulation of Pharmaceutical Promotion." *Globalization and Health* 8: 24.
- Lexchin, J. 2012b. "New Drugs and Safety: What Happened to New Active Substances Approved in Canada between 1995 and 2010?" *Archive of Internal Medicine* 172: 1680–81.
- Lexchin, J. 2014. "Postmarket Safety Warnings for Drugs Approved in Canada Under the Notice of Compliance with Conditions Policy." *British Journal of Clinical Pharmacology* 79(5): 847–59.
- Lexchin, J. 2016. "How Safe and Innovative are First in Class Drugs Approved by Health Canada: A Cohort Study." *Healthcare Policy* 12(2)6: 65–75. doi:10.12927/hcpol.2016.24851.
- Lexchin, J. and B. Mintzes. 2014. "A Compromise Too Far: A Review of Canadian Cases of Direct-to-Consumer Advertising Regulation." *International Journal of Risk and Safety in Medicine* 26: 213–25.
- Light, D., J. Lexchin and J. Darrow. 2013. "Institutional Corruption of Pharmaceuticals and the Myth of Safe and Effective Drugs." *Journal of Law, Medicine & Ethics* 41: 590–600.
- McKinnell, H. 2005. *A Call to Action: Taking Back Healthcare for Future Generations*. New York, NY: McGraw Hill.
- Michols, D. 1997. *Drugs and Medical Devices Programme Quality Initiative Bulletin #2*. Ottawa, ON: Health Protection Branch.
- OECD. 2015. "Health at a Glance 2015: OECD Indicators." Retrieved February 21, 2016. <http://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2015_health_glance-2015-en>. doi:10.1787/health_glance-2015-en.
- Olson, M.K. 2002. "Pharmaceutical Policy Change and the Safety of New Drugs." *Journal of Law and Economics* 45: 615–42.
- Spurling, G., P.R. Mansfield, B. Montgomery, J. Lexchin, J. Doust, N. Othman and A. Vitry. 2010. "Information from Pharmaceutical Companies and the Quality, Quantity, and Cost of Physicians' Prescribing: A Systematic Review." *PLoS Medicine* 7: e1000352.
- 't Hoen, E. 2016. *Private Patents and Public Health: Changing Intellectual Property Rules for Access to Medicines*. Amsterdam, NL: HAI.