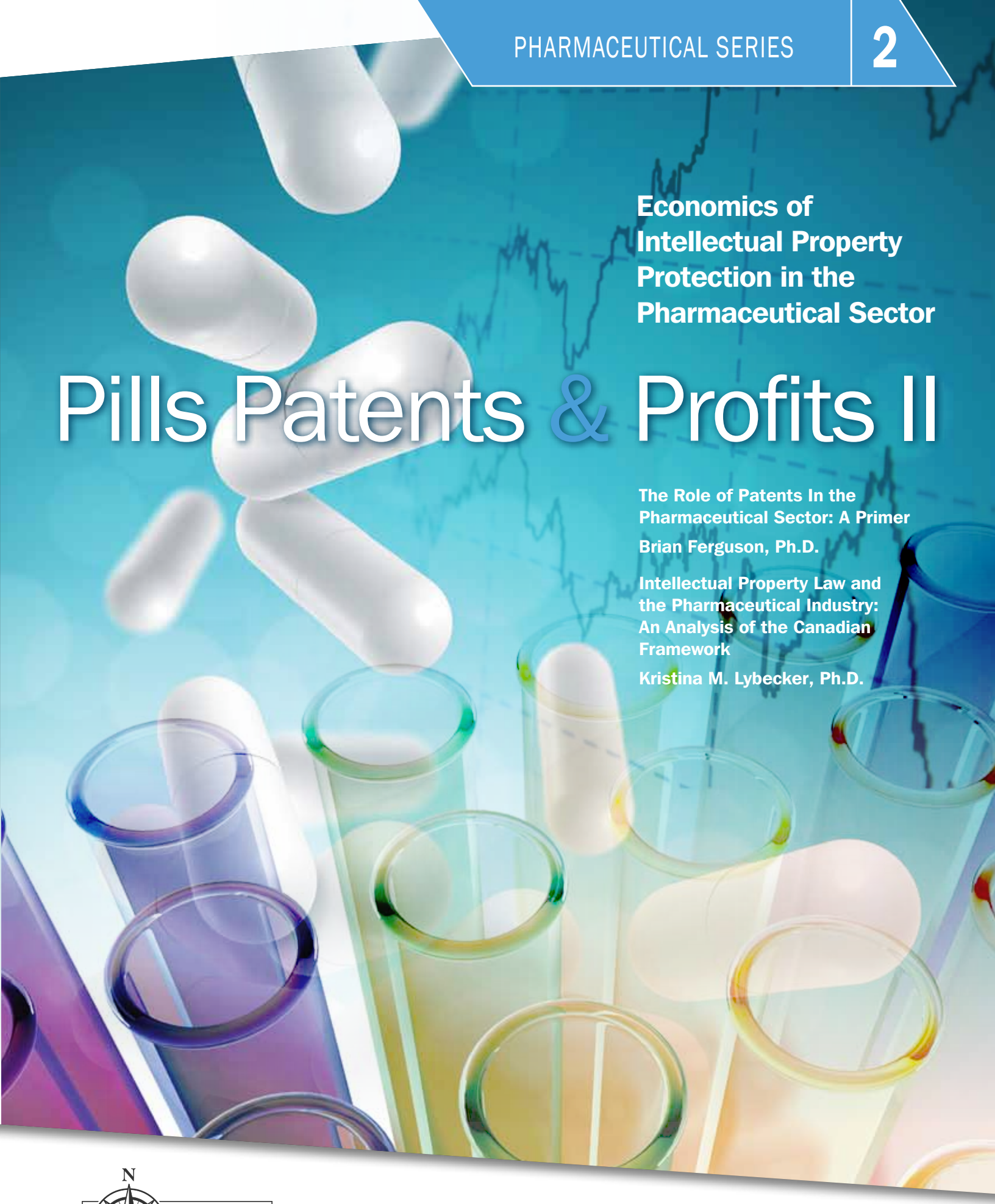

Economics of Intellectual Property Protection in the Pharmaceutical Sector

Pills Patents & Profits II

The Role of Patents In the Pharmaceutical Sector: A Primer

Brian Ferguson, Ph.D.

Intellectual Property Law and the Pharmaceutical Industry: An Analysis of the Canadian Framework

Kristina M. Lybecker, Ph.D.

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Executive Summary

Are pharmaceutical patents essential for the advancement of research, or do they stand in the way of ensuring that life-saving drugs are available where they are most needed? The funds for expensive pharmaceutical research must come from somewhere. One school of thought says that without the temporary monopoly revenue that patents offer, pharmaceutical research and the resulting therapeutic advances would be dramatically reduced. Others argue that pharmaceutical patents prevent innovative therapies from reaching patients, and that much of the research is completed at publicly-funded universities. Understanding the costs and benefits of patents and their protection through intellectual property rights is paramount in getting the balance right for patent protection.

Understanding the costs and benefits of patents and their protection through intellectual property rights is paramount in getting the balance right for patent protection.

In *"The Role of Patents: A Primer,"* Professor Brian Ferguson provides a comprehensive review of research regarding patents and alternatives. He outlines, for example, the stages of drug development and summarizes the key features of the pharmaceutical patent system. He points out that many innovative approaches and alternatives to patents have been proposed. While many of them are worth considering, most research seems to indicate that despite its costs and flaws, the patent system is probably still the best mechanism for encouraging pharmaceutical R&D.

In *"Intellectual Property Law and the Pharmaceutical Industry: An Analysis of the Canadian Framework,"* Professor Kristina Lybecker recognizes that because the pharmaceutical research and development process is lengthy, expensive, uncertain, and risky, pharmaceutical firms rely disproportionately on patents and other forms of intellectual property protection to ensure that they receive sufficient returns to cover the costs they have incurred. However, while patent protection for both pharmaceutical products and processes has become the global norm, significant differences exist across national legal frameworks for the protection of pharmaceutical intellectual property.

Lybecker analyzes these differences in IP protection across the seven regions with the highest levels of research and development spending by PhRMA member companies: Canada, the United States, the European Union, South Korea, Japan, Australia, and Brazil. The most significant differences across regimes appear to be in the areas of patent term extensions (where Canada is an outlier without legislation), price regulation of patented drugs (where the United States is an outlier without

legislation), and basic patent linkage with automatic injunction (where Canada, the United States, and Australia have provisions in place while the European Union, South Korea, and Japan do not). By comparing international norms and policies in each country, Lybecker evaluates the characteristics of the legal framework that will best encourage pharmaceutical industry growth and applies the lessons to Canada.

The paper provides four specific recommendations that will further strengthen Canada's legal architecture for intellectual property protection and thus encourage pharmaceutical innovation in this country.

First, because Canada is one of the few industrialized nations lacking a policy for rare diseases, the country should implement *orphan drug legislation*. Legislation designed to encourage the development of treatments for rare diseases was passed in the United States in 1983, introduced in Japan in 1993, in Australia in 1997, and in the European Union in 1999. Such legislation in Canada would define a "rare disease" and incentivize Canadian firms to intensify their research and develop efforts to discover new therapies for these diseases.

Canada needs orphan drug legislation to encourage R&D for rare diseases.

Second, Lybecker encourages more expansive *data exclusivity protection*. Currently in Canada, while innovative drugs are protected from generic competition through the protection of innovator data for eight years, only drugs meeting certain criteria are eligible. In addition, data exclusivity currently does not apply to new uses for existing drugs in Canada. Strengthening data exclusivity laws will give innovative firms the incentives to produce the data required for regulatory approval.

Patent protection needs to be extended to accommodate for delays from regulatory approval.

Third, unlike most other nations, Canada fails to provide an extra period of patent protection as compensation for time lost due to regulatory approval delays. This is an area where Canada differs significantly from the United States and the European Union. Lybecker recommends legislation granting a potential *patent term extension* to innovator firms in order to recoup the time spent attaining regulatory and marketing approval. The restoration of zero to five years, as is the practice in other jurisdictions, would lengthen the effective patent life of innovative therapies, increasing the incentives to invest in the research and development costs that these treatments require.

Patent protection needs to be extended to accommodate for delays from regulatory approval.

Fourth and finally, Lybecker suggests that Canada strengthen its *anti-counterfeiting legislation*. Criminal sanctions in concert with regulatory provisions will safeguard the health of patients and protect the pharmaceutical industry from the theft of intellectual property and the threat of fraudulent medicines. Through the protection of the industry's research and development investments, additional innovation would be incentivized. In addition, such legislation would more closely align Canada with the Council of Europe which recently adopted the "Medicrime" Convention on pharmaceutical counterfeiting and similar crimes involving threats to public health. That legislation aims to strengthen product protection measures, ensure reliability in the wholesale distribution of pharmaceuticals, and define clear obligations for starting materials.

Although each of the legal environments considered in Lybecker's chapter complies with WTO obligations and other multinational conventions, it is possible to distinguish where protection most advances a vigorous, innovation-based pharmaceutical industry. Of course the appropriate legal framework will depend on the type of industry that one hopes to foster. Clearly the legislation that facilitates the growth of a prospering generic industry differs from that which nurtures a robust innovation-based industry.

Sommaire

Les brevets pharmaceutiques sont-ils essentiels à l'avancement de la recherche, ou sont-ils un obstacle à ce que les médicaments qui sauvent des vies soient disponibles là où on en a le plus besoin? Les fonds pour financer la coûteuse recherche pharmaceutique doivent venir de quelque part. Selon une école de pensée, la recherche pharmaceutique et les avancées thérapeutiques qui en résultent seraient considérablement réduites sans les revenus monopolistiques temporaires que permettent les brevets. D'autres soutiennent que les brevets pharmaceutiques empêchent les patients d'avoir accès aux thérapies innovantes, et qu'une bonne partie de la recherche se fait de toute façon dans des universités financées par l'État. Si l'on veut obtenir le meilleur équilibre possible au chapitre de la protection des brevets, il est crucial de comprendre les coûts et les bénéfices qui en découlent et comment ceux-ci sont garantis par des droits de propriété intellectuelle.

Si l'on veut obtenir le meilleur équilibre possible au chapitre de la protection des brevets, il est crucial de comprendre les coûts et les bénéfices qui en découlent et comment ceux-ci sont garantis par des droits de propriété intellectuelle.

Dans *The Role of Patents: A Primer*, le professeur Brian Ferguson propose une revue exhaustive de la recherche en ce qui a trait aux brevets et à leurs solutions de rechange. Il esquisse ainsi les étapes du développement d'un médicament et résume les principales caractéristiques du système de brevet pharmaceutique. Il souligne que plusieurs approches innovatrices and solutions de rechange aux brevets ont été proposées. Bien que plusieurs d'entre elles méritent d'être examinées, la plupart des études semblent indiquer que malgré ses coûts et ses failles, le système de brevet est probablement toujours le meilleur mécanisme pour encourager la R&D pharmaceutique.

Dans *Intellectual Property Law and the Pharmaceutical Industry: An Analysis of the Canadian Framework,* la professeure Kristina Lybecker reconnaît que comme le processus de recherche et développement des médicaments est long, coûteux, incertain et risqué, les compagnies pharmaceutiques comptent de manière disproportionnée sur les brevets et d'autres formes de propriété intellectuelle pour s'assurer de recevoir un rendement suffisant pour couvrir les coûts encourus. Cependant, même si une protection au moyen des brevets est devenue la norme mondiale autant pour les produits que pour les processus de production pharmaceutiques, des différences significatives existent d'un cadre juridique national à l'autre en ce qui a trait à la protection de la propriété intellectuelle dans le domaine pharmaceutique.

Mme Lybecker analyse ces différences entre les sept régions du monde où l'on retrouve les plus hauts niveaux de dépense sur la recherche et le développement par des compagnies membres de PhRMA : le Canada, les États-Unis, l'Union européenne, la Corée du Sud, le Japon, l'Australie et le Brésil. Les principales différences entre les différents régimes semblent toucher les questions du prolongement de la durée des brevets (le Canada étant le seul pays sans législation), la réglementation des prix des médicaments brevetés (les États-Unis étant également le seul pays sans législation) et un lien de base entre les brevets et l'obtention d'une injonction automatique (dans ce cas, le Canada, les États-Unis et l'Australie ont des mesures en place, alors que l'Union européenne, la Corée du Sud et le Japon n'en ont pas). En comparant les normes et les politiques de chaque pays, Mme Lybecker évalue les caractéristiques du cadre juridique qui encourageront le plus la croissance de l'industrie pharmaceutique et applique ces leçons au Canada.

L'étude propose quatre recommandations spécifiques pour renforcer le cadre juridique de la propriété intellectuelle au Canada et ainsi encourager l'innovation pharmaceutique.

Premièrement, en tant que l'un des rares pays industrialisés n'ayant pas de politique sur les maladies rares, le Canada devrait adopter une *loi sur les médicaments orphelins*. Des lois visant à encourager le développement de traitements pour les maladies rares ont été adoptées aux États-Unis en 1983, au Japon en 1993, en Australie en 1997 et dans l'Union européenne en 1999. Une telle loi, si elle était adoptée au Canada, permettrait de définir ce qu'est une « maladie rare » et d'inciter les firmes canadiennes à intensifier leurs recherches et à développer leurs efforts pour découvrir de nouvelles thérapies contre ces maladies.

Le Canada a besoin d'une loi sur les médicaments orphelins pour encourager la R&D visant les maladies rares.

Deuxièmement, Mme Lybecker propose une protection accrue de *l'exclusivité des données*. En ce moment au Canada, les médicaments innovants sont à l'abri de la compétition des médicaments génériques par une protection d'une durée de huit ans des données de l'innovateur, mais seuls sont éligibles les médicaments qui satisfont à certains critères. De plus, l'exclusivité des données ne s'applique pas aux nouvelles utilisations pour des médicaments existants au Canada. Renforcer la loi sur l'exclusivité des données donnerait aux firmes innovatrices l'incitation à produire les données requises pour l'approbation réglementaire.

La protection que confère le brevet doit être allongée pour tenir compte des délais de l'approbation réglementaire.

Troisièmement, au contraire de la plupart des autres pays, le Canada ne permet pas de période supplémentaire de protection par le brevet pour compenser le temps perdu à cause des délais d'approbation réglementaire. C'est un domaine où la législation canadienne diffère grandement de celle des États-Unis et de l'Union européenne. Mme Lybecker recommande l'adoption d'une loi accordant potentiellement une prolongation de la durée du brevet aux firmes innovatrices pour récupérer le temps passé à tenter d'obtenir une approbation réglementaire et de mise en marché. Cette remise d'une à cinq années, comme c'est le cas dans d'autres juridictions, allongerait la durée de vie effective du brevet des thérapies innovantes, augmentant ainsi les incitations à investir dans les coûts de recherche et développement que requièrent ces traitements.

La protection que confère le brevet doit être allongée pour tenir compte des délais de l'approbation réglementaire.

Enfin, Mme Lybecker propose que le Canada renforce sa *législation contre la contrefaçon*. Des sanctions criminelles, de concert avec des mesures réglementaires, permettront de protéger la santé des patients et de mettre l'industrie pharmaceutique à l'abri du vol de propriété intellectuelle et de la menace de médicaments frauduleux. On encouragerait davantage l'innovation en protégeant les investissements en recherche et développement de l'industrie. De plus une telle loi alignerait plus étroitement le Canada sur le Conseil de l'Europe, qui a récemment adopté une convention « Medicrime » contre la contrefaçon pharmaceutique et des crimes similaires impliquant des menaces à la santé publique. Cette loi vise à renforcer les mesure de protection des produits, garantir la fiabilité de la distribution en gros des médicaments et définir des obligations claires pour les matières premières à usage pharmaceutique.

Bien que chacun des environnements juridiques passés en revue dans le chapitre de Mme Lybecker soit en conformité avec les obligations de l'OMC et d'autres accords multinationaux, il est possible de distinguer ceux où la protection est la plus susceptible de mener à une industrie pharmaceutique vigoureuse et fondée sur l'innovation. Le cadre juridique approprié dépendra bien sûr du type d'industrie que l'on souhaite voir se développer. Il est clair qu'une législation qui facilite la croissance d'une industrie générique dynamique diffère d'une autre qui aide au développement d'une solide industrie fondée sur l'innovation.

The Role of Patents in the Pharmaceutical Sector: A Primer

Brian Ferguson, Ph.D.

Introduction to Patents and Patenting

The role of patents, and intellectual property in general, in the pharmaceutical sector, is one of the more contentious policy areas in economics. Depending on one's point of view, pharmaceutical patents are either absolutely essential for the advancement of research or they are the major obstacle to making life-saving drugs available where they are most needed. This debate inevitably overlaps with another: that about the funding of pharmaceutical research. Proponents of patents argue that without the temporary monopoly revenue that they yield, pharmaceutical research would come to a halt – that they are, in short, essential to foster productive entrepreneurship; opponents argue that most pharmaceutical research is done at government-funded institutions and that the research-based pharmaceutical sector is in fact nothing but a marketing sector, free-riding on publicly-funded research. Opponents of patents also argue that much patenting activity is aimed at securing patent protection for me-too (copycat) drugs, or at evergreening, (stretching out patent life by making minor changes to existing drugs), and not at bringing truly innovative drugs to market – that they are fostering unproductive entrepreneurship.

Patents and intellectual property are contentious policy areas.

More broadly, the patent system in general, and not just that bit of it that applies to pharmaceuticals, has fallen into public disrepute in recent years. In part this is because of the willingness of patent offices (especially, in the public's mind, the US Patent and Trademark Office, or USPTO) to issue patents for ideas that most people would consider unpatentable. In other words, for many people, the patent offices in various countries are far too willing to facilitate unproductive entrepreneurship.

At one level, this mistrust is the result of reports that the US Patent Office has issued patents for things like starship warp drives (this may be a myth, and on at least one occasion it seems that a patent examiner rejected a warp drive patent because the applicant didn't submit a working model). More seriously, patent fights over business methods have raised questions about what should be patentable, and also about which things should be patentable and which copyrightable, a matter which to some degree overlaps the issue of product versus process patents.

Productive and Unproductive Entrepreneurship

Productive and unproductive entrepreneurship are terms introduced by William J. Baumol as extensions of Joseph Schumpeter's concept of creative destruction.[1] The *creative* part of creative destruction refers to activity that enables societies to make significant advancements, ultimately to the benefit the whole of society. The *destruction* part of creative destruction refers to the fact that these steps are not costless, and that the cost includes both the immediate accounting costs of bringing the new activity into existence and the costs incurred by the sectors made obsolete by the creative advance. Computers wiped out a large part of the typewriter industry, for instance, but were a significant improvement over the older sector, if only because of the ability to cut, paste, and make corrections without having to use whiteout or re-type entire pages. In Baumol's schema, productive entrepreneurship is the basis of creative destruction.

Unproductive entrepreneurship, on the other hand, refers to what economists also term "rent-seeking activity": devoting resources to finding ways to transfer wealth from others to yourself, usually through the activities of governments. It involves persuading governments to grant protection to your activities, sometimes against domestic competitors by granting a domestic monopoly, and sometimes against foreign competitors by putting in place tariff and quota protection. If a firm can convince its country's government that it should be regarded as a domestic champion, it is likely to be able to obtain protection from both domestic and foreign competitors. That kind of monopoly position can be extremely lucrative, so firms are often prepared to devote considerable resources – to engage in large-scale unproductive entrepreneurship – to obtain it. Depending on the degree to which rule of law is a meaningful concept in a country, this form of activity can range from lobbying to bribery.

Every society possesses a stock of entrepreneurial talent; the question is how it is used.

Baumol argues that every society possesses a stock of entrepreneurial talent; the key question is how it used. Entrepreneurial abilities will be directed towards either productive or unproductive activities depending on where the returns are expected to be greater. Accordingly, the single most important type of industrial policy that a country can introduce is one that makes productive entrepreneurship consistently more profitable than unproductive entrepreneurship.

The Historical Setting

It is no exaggeration to say that the industrial organization of the modern pharmaceutical sector was largely shaped by a key patent decision.

By "modern pharmaceutical sector," we are referring to the post-penicillin industry. Penicillin itself was not patented (as the product of a fungus, penicillin was quite possibly not patentable since mouldy bread had been used to treat wounds since the Middle Ages – hence it was an issue of "prior art", meaning that a certain amount was already known about its therapeutic effect), but the antibiotics that followed it were. The key to the changeover was the patentability of streptomycin (Kingston 2000). The primary issue about the

1 On creative destruction, see Schumpeter, 2008 (orig. pub. 1942). On productive and unproductive entrepreneurship, see Baumol, 1990.

patentability of streptomycin was that it was a product of a natural organism, an actinobacterium. The fact that tipped the ruling in favour of streptomycin being patentable was the amount of work needed to convert the original living organism into a usable broad-spectrum antibiotic.[2]

Drug discovery and development run through a series of reasonably clearly defined stages.

The ruling ensured that pharmaceutical companies stood a reasonable chance of recovering the costs of discovering and testing similar antibiotics and making a profit, and so it encouraged further research. Arguably, the patentability of streptomycin turned the drug industry in the United States from something akin to the modern generic drug sector (in which manufacturers of drugs take advantage of the research emerging from other sources) into a research-based industry that now spends a larger part of its revenue on research and development (R&D) than does virtually any other industrial sector, with the possible exception of the software development sector.[3]

The Stages of Drug Development

Before we proceed to the discussion of policy issues, a bit of background on how drug development works. Drug discovery and development run through a series of reasonably clearly defined stages. The first is the pre-clinical stage. It is here where research, including basic laboratory research and animal research that does not involve human subjects takes place. This is the stage at which the vast majority of what looked to be promising avenues fail. The commonly used figure is that for every 5,000 to 10,000 compounds investigated in the pre-clinical stage, one will make it to market. A significant amount of this first stage of research is done at universities and other research bodies outside the pharmaceutical sector. That work is, to a large degree, what critics of the pharmaceutical sector are referring to when they talk about Big Pharma free-riding on government funded research.

Studies have determined the proportion of marketed drugs developed from work done at universities and found it to be quite appreciable. However, this is the wrong metric. These studies have looked at the probability that a marketed drug has university-based research in its background. The correct conditional probability involves looking at the probability that any given piece of university-based research will lead to a marketable drug. On that metric, judging from the number of promising compounds that do not make it past animal testing, the numbers look less favourable.

Critics sometimes imply that dozens of viable drugs sit in university labs, ignored by the pharmaceutical sector. This is not a credible argument, especially from those whose main objection to the research-based pharmaceutical sector is that companies are only interested in profits. It amounts to claiming that these companies (a) will free-ride on anyone to make money, but (b) are leaving thousands of dollars-worth of profitable drugs that they know about to gather dust in university labs. In other words, Big Pharma is both greedy and stupid.

2 As a matter of interest, although the license to streptomycin belonged to Merck, which had financed the research at Rutgers University which led to the discovery, Merck agreed to return it to Rutgers (which had already made a considerable sum as its share of Merck's even more considerable profits) to fund a research institute, and Rutgers began issuing non-exclusive licenses for the production of antibiotics. In a foreshadowing of the world of generic drugs, the profitability of the original output of streptomycin attracted so many new producers that the price plummeted and quite a number of suppliers lost money producing a blockbuster wonder-drug. The plummeting prices also cut off Rutgers' revenues for the research institute.

3 On the history of the US drug sector, see Temin, 1980.

If a drug candidate survives pre-clinical testing, it enters the human testing stage. This is broken into three phases.

- In Phase I trials, the drug candidate is administered to a small number of subjects to monitor and test for adverse effects. If these are absent or minimal, the drug moves on to Phase II.

- In Phase II trials, the drug candidate is given to a relatively small number of subjects to see whether, when given to humans, it still seems to deliver its intended benefits. The number of subjects involved is generally too small to yield statistically strong results, so Phase II trials really serve as a decision node – whether to proceed to larger human trials or whether to stop work. It is not unusual for a drug candidate to be dropped at this stage. While animal trials are essential to evaluate whether a drug is likely to work in humans, animals and humans are different. A drug that works in one species does not necessarily work in another. The news media have announced many a breakthrough in cancer treatments, only for that breakthrough never to be heard of again. Apparently, it is much easier to cure cancer in rats than it is in humans.

The commonly used figure is that for every 5,000 to 10,000 compounds investigated in the pre-clinical stage, one will make it to market.

- If the Phase II results are promising, the drug candidate moves on to Phase III trials. This phase involves a large-scale trial in humans to see whether the drug's promise holds up. Phase III trials can involve several thousand subjects, half of whom are randomly assigned into the control group (who receive the current standard treatment for the disease) and half into the treatment group (who are treated with the drug candidate). The duration of the trial depends on the nature of the disease, but it can last several years. Only if a drug makes it through all three trial phases to the satisfaction of the relevant regulatory authority (the Food and Drug Administration (FDA) in the US and Health Canada in Canada) can it be approved for sale. Phase III trials have evolved into the largest and most expensive part of drug development for two main reasons.

    1) One is increased concern for safety and side-effects. While the Phase I trial tells researchers whether taking the drug kills subjects quickly, it takes a large and relatively long trial to determine whether serious, possibly fatal, side-effects will appear in a statistically significant number of people taking the drug (that is, significantly more than would appear in the population at large).

    2) The other is that the easy work has already been done. Modern drug research focuses on mechanisms (the interaction of the drug with the body that produces the pharmacological effect) and diseases that are different from those involved in earlier research into compounds like antibiotics. Therapies advance incrementally, so it is common for a drug to affect only a subset of the target population. The result is that larger trials are needed to test whether a treatment has a clinically significant impact on a statistically significant subset of the population.

Recovering Drug Development Costs

All of these trials and phases are costly, and a key issue in the debate about patent policy is whether patents are the best way to allow the pharmaceutical sector to recover its research and development costs[4]. Statements about cost recovery are not uncontroversial, in part because of disagreements about how high those costs

4 For a discussion of a range of theoretical issues related to patents and the recovery of research costs, see Tabarrok (2002).

actually are. The most widely used figure is on the order of US$800 million, but some commentators argue that the true figure is smaller, closer to US$100-200 million. In assessing the arguments in this literature, it is important to remember that drugs that make it to market must fund a pharmaceutical company's entire research and development activity, i.e., the successful drugs must pay the costs of the promising directions that turned out to be blind alleys. Given the rate of attrition, even in the clinical trial phase, this is a considerable amount. A drug that makes it all the way through to the end of Phase III before failing, as seems, on the latest evidence, to be the case with Teva's Multiple Sclerosis drug laquinimod (strictly speaking, laquinimod fell short of its targets, and as of this writing the data is being reanalyzed, and may still be submitted for FDA approval) can have racked up hundreds of millions of dollars in development costs which the company will not be able to recover. When Pfizer dropped torcetrapib, a cholesterol drug, because of elevated mortality among Phase III trial subjects, it was reported that it had spent US$800 million on developing the drug (Cutler 2001).

Recent analysis (Arrowsmith 2011a and 2011b) of Phase II and Phase III outcomes suggests that only about 18 percent of drugs survive Phase II, and that only about 50 percent of those that advance from Phase II to Phase III make it through to market launch. Failing in Phase II is considerably less expensive than failing in Phase III, but the much higher failure rate in Phase II (70-80 percent in recent years) means that pharmaceutical companies must have large numbers of drugs under investigation if they hope to bring new drugs to market on a regular basis. Most commentators think that the productivity of the drug R&D enterprise has dropped significantly in the past decade, in part, as noted above, because the science is quite different from that required to deal with older targets.

Even if a drug makes it to market, there is no guarantee that it will be financially successful.

Even if a drug makes it to market, there is no guarantee that it will be financially successful. For example, Pfizer spent a considerable sum on developing and marketing Exubera, an inhalable insulin product, only to find that doctors were not satisfied with the drug and that patients did not like the inhaler, which was reported to be the size of a can of hairspray. Pfizer dropped Exubera altogether in 2007, taking a reported write-off of over US$2 billion on it. Shortly afterward, Novo Nordisk and Eli Lilly ceased development on their own experimental inhalable insulin products. As of 2011, the only inhalable insulin product left in trials is MannKind's Afrezza, which has cost a lot to develop and keeps running up against FDA requests for further data (Rubenstein 2008).

Roughly only 30 percent of drugs actually make it to market and generate revenues.

Only an estimated 30 percent of drugs that actually make it to market generate enough revenue to contribute significantly to the industry's R&D enterprise, meaning that the ability to develop new drugs has relied on having found "blockbusters" in the past. Some commentators regard this dependence as a new feature of the pharmaceutical sector, and argue that the

pharmaceutical sector's blockbuster mentality has been an obstacle to developing drugs for diseases that affect small segments of the population – blockbusters by implication are mass market drugs. In fact, the nature of the pharmaceutical sector is that the distribution of profits has always been highly skewed.[5]

What all of this comes down to is the fact that drug development, at the level of the individual drug, is a long-term and risky investment project. Large pharmaceutical companies have, in the past, tended to be shielded by having large portfolios of drugs, some on the market and some under development, with new drugs in the pipeline to replace ones nearing the end of their profitable lives. Of late, though, there has been concern that the pipeline is drying up.

Scherer (2001) has shown that pharmaceutical R&D spending moves practically in lockstep with earnings, with the causality running from earnings to R&D. If we needed any more evidence, it is notable how, as Big Pharma's profits have fallen, the industry has been quick to retrench in its R&D operations. In other words, Big Pharma's research activities are driven by Big Pharma's ability to retain earnings. Does that, however, justify claims about the importance of patent protection for ongoing pharmaceutical research activity?

Roughly only 30 percent of drugs actually make it to market and generate revenues.

Product Patents Versus Process Patents

Before answering that question, we need to take a look at the way patents work in the pharmaceutical sector. There are two broad types of patents: product patents and process patents. Product patents cover the product itself, regardless of how it is made. Process patents apply to particular ways of producing a final product, but not to the product itself. Process patent protection is therefore weaker than product patent protection – if a competitor can come up with a different way of producing an existing drug, they can bring their version to market without violating the originator's process patent. Under a product patent, the patent holder has a monopoly for a particular product for a fixed period of time.

During that period, the patent holder can exploit his position by charging a monopoly price and making monopoly profits on the product. The role of these profits is twofold: first, they allow the patent holder to recover what he spent on developing the patented product, and second, they signal to potential entrants that profits can be made on the product. That in turn attracts competition into the market which, though delayed to some degree until the original patent expires, ultimately drives down the price of the product, transferring most of the welfare gain from the introduction of the new product to consumers and leaving producers with a normal economic profit.[6]

The basic conundrum of patent theory is to determine the optimal life of a patent – one long enough to allow the patent holder to recover his costs and make a profit large enough to convince others that it is worthwhile to devote resources to innovation, but not so long that the entry of competitors is delayed beyond the socially efficient period. From the perspective of social welfare, patent protection should be just enough to encourage productive entrepreneurship but not so long as to allow the patent holder to reap his monopoly revenue without undertaking any further productive entrepreneurial activity.

5 See, for example, Scherer 1996. On related issues, see Scherer and Harhoff 2000.

6 For a broad perspective on where the gains from innovation wind up, see Nordhaus 2004.

Similarly, the degree of patent protection should be sufficient to reward entrepreneurship, but not so protective that it closes the door on someone else finding a different way of satisfying the same consumer want and entering the market with that new product. Pharmaceutical patents in Canada extend for 20 years from the date when the patent is filed. This sounds as though it should provide more than enough monopoly protection to enable patent holders to recover their costs, but there is a catch. Pharmaceutical companies typically file for patent protection very early in the development process rather than wait until the drug approaches marketability, because they do not want to risk a competitor filing before they do. If they do leave filing until late in the clinical trial process and a competitor files before they do, they will lose their development costs on that drug up to that point. Rather than run the risk, pharmaceutical companies file as soon as a drug candidate shows real promise. The result is that, by the time a drug is marketable, there may only be seven years of patent protection left – the rest having been consumed by the clinical trials process. The company must therefore recover the drug's development costs within that seven years.

Pharmaceutical patents in Canada theoretically extend for 20 years from the date when the patent is filed.

This, finally, brings us back to the question of whether the evidence justifies claims about the importance of patent protection for ongoing pharmaceutical research activity. Some authors argue that it does not. Boldrin and Levine (2008), for example, make the point that the pharmaceutical industry grew up, for the most part, in countries that did not permit patenting of pharmaceuticals (although they acknowledge that those companies were diligent about patenting their products in countries that did permit it) at the time. They also cite research by Scherer and Weisbrod (1995) showing that the introduction of pharmaceutical patents in Italy in 1978 did not result in a surge in innovation and patenting. In their review, however, Boldrin and Levine do not deal with a key point made by Petra Moser (2007, 2011) (whose work they cite) about why the pharmaceutical sector changed from one in which patents were not much used to one in which patenting is the primary mechanism by which the industry reaps the returns from its innovative efforts.

Moser and others have looked at how companies appropriate the profits from their innovative efforts. The mechanisms used vary depending on the nature of the industry, however, patents tend to be low on the list of useful mechanisms in most sectors. A lot of mechanical innovations, for example, are never patented because patents for that type of item are too easy to circumvent.

Patents vs. Secrecy

A patent has to describe the key elements of an innovation. However, making that information public would give competitors a head start in finding another way of doing the same thing in a way that differs just enough from the original innovation to avoid violating the patent. Sometimes firms prefer to rely on secrecy to protect their position. This can work: the precise formula for Coca Cola has never been patented, but has been kept secret. The basic elements of the recipe are apparently widely known; what's not known is the precise mix, and it is the mix of ingredients that gives a soft drink its distinctive taste. Had Coke been patented, its patent would have expired long ago and anyone who wanted to would be able to produce their own exact copy of Coke (although they wouldn't be able to sell it in bottles identical to Coke bottles – that design is trademarked). According to Moser, the pharmaceutical sector was content to rely on secrecy to protect its intellectual property until the science of chemistry advanced to the point where reverse engineering of drugs became feasible – i.e., to the point where it became possible to take a drug apart and sort out exactly

how it was made. Once analytical chemistry reached that stage, a pharmaceutical secret would last only as long as it took a chemist to analyze a few of the new pills. It was, according to Moser's research, at that stage that the pharmaceutical sector shifted from relying on secrecy to relying on patents to protect its intellectual property. (That also suggests, incidentally, that the chemical composition of Coca Cola is in some sense more complicated than that of a whole lot of drugs, since the formula for Coke is still a secret.)

So while it is true, as Boldrin and Levine argue, that the pharmaceutical sector began and grew strongly in countries that did not permit its products to be patented, it is also true that it shifted over to using patents as a device for protecting intellectual property, which many industries did not. Presumably it would only have switched to going through the process of getting patents (in countries where it became possible to obtain them) if the return from doing so exceeded the return to using some other method to protect its innovations, and Moser's evidence suggests that the switch was indeed a rational, profit-maximizing decision by the research-based industry.

Still, the question remains as to whether any direct evidence exists of patenting actually stimulating research activity, as opposed simply to allowing pharmaceutical companies to reap the profits from discoveries that it stumbles upon or that somebody else makes. The answer is yes.

According to Moser, the pharmaceutical sector was content to rely on secrecy to protect its intellectual property until the science of chemistry advanced to the point where reverse engineering of drugs became feasible.

The Link Between Patents and Research Activity

We have already seen that drug companies do, in fact, spend considerable amounts on research, even if the details of the assignment of particular total economic sums to particular drugs (i.e., how much it costs in R&D to bring a drug successfully to market) are subject to debate. As we have noted, Scherer has adduced evidence that pharmaceutical R&D spending depends on gross profitability, and the source of those earnings is the monopoly profit the drug companies make on those relatively few patented drugs that earn more than they cost to develop and produce – blockbusters. Both the surge in R&D spending after the 1940s, and the conversion of the industry into a research-based enterprise, were a response to the hope of making streptomycin-level profits on the new, patentable drugs which would come out of that R&D.

There is also evidence that likely inability to obtain or enforce a patent will discourage research in particular areas. Pharmaceutical companies assess the patentability of compounds when considering whether to devote resources to investigating them. Compounds that are regarded as weak from that point of view tend to be dropped before large sums are spent on them. Here, "weak" is an assessment of how patent offices are likely to regard a drug, especially with regard to novelty and the prior existence of information about its compounds. Drugs are not patentable if a significant amount of information (known as "prior art") already exists about their therapeutic effect. The problem is not prior art making a drug unpatentable, it is the uncertainty surrounding the definition of prior art. There have been cases where a patent has been refused on a drug because possible uses of the drug have been discussed in the scientific literature, even though its actual efficacy in treating particular diseases had not been established. Given the amount that pharmaceutical companies spend on clinical trials, they tend to be risk-averse about any factors that might make the compound unpatentable, especially if it proves to be successful.

A related problem arises regarding new uses of existing drugs: cases where a drug being used to treat one disease is found to have promise as a treatment for another. This issue came up in news stories about research at the University of Alberta on Dichloroacetic Acid (DCA) as a treatment for cancer (see http://en.wikipedia.org/wiki/Dichloroacetic_acid). DCA has been around since 1864 and is used in veterinary medicine. Even if it were patentable as a cancer treatment, it would be very difficult to defend the monopoly position. As a result (and taking into account the number of promising cancer treatments which have died in Phase II and III trials), pharmaceutical companies are not interested in incurring the costs of clinical trials to see whether DCA's promise holds up, and the University of Alberta almost certainly cannot afford to do so. Multinational companies have the resources to organize the trials (and to take the risk of doing so) needed to convince regulators that a drug is safe and effective in use in humans, but it must be to their advantage.

Me-too Drugs and Evergreening

Inability to obtain or enforce a patent will discourage research.

Pharmaceutical companies are often accused of devoting considerable resources to gaming the patent and regulatory systems, producing me-too drugs, and evergreening their patents. These charges, which relate to whether the companies are engaging in productive or unproductive entrepreneurship, contain an element of truth, but not as much as those making the charges believe.

The term "me-too" drugs, ironically, is never used to refer to generic drugs, even though those are the only genuinely me-too drugs on the market. Instead, it is used to refer to situations where several research-based companies have brought to market treatments for the same condition. The implication is that later entrants are simply copying the first entrant's drug, and that very little original research is involved in the production of the later entrants. There is also an implication that there are no benefits to patients from having different drugs available to treat the same condition.

Negative claims about me-too drugs tend to be backed up by arguments about the number of drugs in a particular therapeutic category that make it to market in close succession. The argument is that the later drugs copy the first entrant without adding any therapeutic benefit. Most of this evidence is misinterpreted. As DiMasi and Paquette (2004) point out, the period between the entry of the first drug and the entry of competitors has been getting shorter over time. One of the benefits of a product patent system is that companies cannot make trivial changes to the way a drug is produced and obtain a patent on that new version. Under this system, a company wanting to enter a market that has existing drugs must devise a compound with a different mechanism from that of the existing drugs. Then, because the drug is not simply a bioequivalent generic, the company must take this new drug through the entire clinical trials process. At present, the gap in time between the first and competing entrants is simply not sufficient to allow this to happen. This means that later drugs are not just copies inspired by the first entrant, but rather are the result of parallel research tracks.

Pharmaceutical companies tend to turn their attention to tackling similar diseases at roughly the same time. The existence of patents forces them to find their own approach to tackling those diseases, and the information contained in the patents filed by others tells them what mechanisms to avoid. Because the later entrants have to work by different mechanisms than do the first entrants, they will have different side-effects

and affect different patients differently. Critics of the pharmaceutical companies tend to dismiss these last two arguments, but in doing so they also implicitly dismiss the field of pharmacogenetics and the idea of personalized medicine, which rests on the notion that something, probably genetic, causes individual A to respond to drug 1 and individual B to drug 2. The major barrier to personalized medicine at the moment is that the genetic factors determining which patient responds to which drug are not known: the only way to personalize a patient's drug treatment is to try different drugs and see which one works best. To do that, a range of drugs (including older, off-patent ones) must be available.

Evergreening refers to the practice of stretching out the lives of patents and preventing manufacturers of generic drugs from entering the market by making very minor changes to existing drugs – from a pill to a caplet to a capsule, for example – and claiming new patent protection for each change. A lot of commentators confuse me-too and evergreening. The two concepts need to be considered as different but related ideas.

Evergreening refers to the practice of stretching out the lives of patents and preventing manufacturers of generic drugs from entering the market by making very minor changes to existing drugs.

Criticisms of evergreening have considerable force. Pharmaceutical companies do devote a lot of resources to extending their patents to prevent competition from manufacturers of generic drugs. But this happens only in cases where the return on resources spent on lawyers and lobbyists is greater than that spent on R&D. At some point, this kind of activity can pass into the realm of unproductive entrepreneurship. Where that point is found, though, remains unclear. Some critics would prevent pharmaceutical companies from obtaining patents on any incremental improvements, and permit new patents only on changes that are significant clinical improvements. However, this deprives patients of incremental benefits they might derive from incremental improvements. Some people find it easier to swallow a capsule than a caplet or a pill. Why should they not have that option, even if the therapeutic benefits of the different forms are identical? One can argue that the pharmaceutical company should have waited until all three forms were ready, but delays associated with developing different delivery mechanisms for the same drug would cut into its patent life and reduce the time left to recoup the research costs. Pharmaceutical companies undoubtedly start working on such variations before the first version of the pill becomes available on the market, but they have to make a commercial judgement about the best moment at which to offer a pill for sale (not to mention when to send to the FDA and Health Canada the data required to obtain clearance to market the drug in the first place).

One issue to consider is that pharmaceutical companies generally get no credit for the fact that generic drugs exist at all. Once a drug's patent has expired, any manufacturer can produce its own version (different countries have their own rules about first-entrant generics and when competing generics can enter). The patent holder gets no credit for the discovery of the original drug and, more importantly, no revenue from the copycat drug.

One way to prevent evergreening from becoming unproductive entrepreneurship would be to change the patent extension rules without making them more complicated – that is, to clarify the conditions under which patent extension can occur – and at the same time to require that any generic entrant pay a compulsory licence fee to the patent holder. This fee should be sufficient to ensure that the patent holder receives a stream of revenue from the drug after the patent has expired, but not so much that the incentive to continue R&D is eliminated.

The Disadvantages of Patents and Alternatives to Them

Even accepting that patents (or some mechanism permitting drug companies to profit from the intellectual property they develop) are necessary to drive the R&D enterprise, they still have disadvantages. The most important of these is that they create monopoly revenues. Monopoly revenues are a problem not because they are large (often they are not) but because a company that has a monopoly position makes a monopoly profit primarily by raising the price above the competitive market level by restricting access to the product. This is why even those economists who support the patent system as a device for increasing social welfare in certain circumstances regard it as what is termed a "second-best mechanism."[7] This is especially so in the case of pharmaceuticals. Monopolies on technologies such as smartphones generate short-run welfare transfers from consumers to producers, but basically act as part of the Schumpeterian process of creative destruction. Some commentators argue that this involves socially wasteful over-investment in smartphone R&D, but the money being invested belongs to the companies' shareholders who are supplying it voluntarily.

In the case of pharmaceuticals, especially for products like cancer drugs, legitimate concern exists about the cost of restricting supply in the short run. Restriction amounts to making a trade-off between the health of people today and the health of even more people in the future. At some point, the patents will expire and the drugs will become much more widely available, but in the interim, some people who would benefit from these drugs today will not get them. With smartphones, the trade-off is not that onerous. With drugs, it may well be; this concern underlies many of the proposals for alternatives to patents to finance drug research.

Pharmaceutical companies generally get no credit for the fact that generic drugs exist at all.

Most proposals for alternatives to patents look for ways of making drugs available at a price close to the cost of production, as opposed to the monopoly price, while still making the equivalent of monopoly rents available to fund future research. The extent to which pricing is taken out of the hands of the pharmaceutical companies varies across the range of proposals – some allow companies to choose whether to opt in to alternative payment mechanisms, retaining the right to stay with the traditional approach for some drugs. A number of proposals have recommended changes to the current system of funding drug research. Broadly speaking, they include replacing patents with prizes, governments buying patents out or otherwise taking them over and compensating their holders, and public funding of clinical trials.[8] They all have merits worth considering, especially as devices for creating incentives for research on neglected diseases, but all need to be examined carefully.

Public Funding of Clinical Trials

It is widely argued that public funding of clinical trials would be superior to the present system because:

- proponents believe that governments can conduct trials at a lower cost than do pharmaceutical companies; and
- knowledge acquired through clinical trials has many features of a public good (as economists use the term, not in the sense of a private good paid out of the public purse) in that it is non-rivalrous (anyone can use

7 A second-best mechanism refers to a situation where no first-best mechanism exists, i.e., where the full set of conditions for welfare maximization cannot be satisfied.

8 On the various alternatives to patents discussed here, see Hollis 2007; Grootendorst 2009; Jayadev and Stiglitz 2008; Kremer 1997; and Grootendorst, Hollis, Levine, Pogge, and Edwards 2010.

the information in their research) and if not completely non-excludable (since others are excluded from it for as long as it is kept secret) at least partially so, since once it becomes available it is impossible to pull back. The only way to treat such knowledge (the information would include discoveries about harmful effects of drugs, which, it is claimed, pharmaceutical companies suppress when they report trial results) as a public good and make it freely and publicly available is for government to fund trials and to own the information from the beginning. In these proposals, the government would recoup the costs of the trials from users of the drug in the form of a small surcharge.

This proposal neglects to address the question of failed trials. Proponents argue that clinical trials cost far less than the $US800 million claimed. This is true – *only* if the cost of trials associated with a drug that makes it to market is considered. The proposal does not take into account all the drugs that fail only after the data from the Phase III trial has been analyzed. Failures outnumber successes these days, even in Phase III trials. It is one thing for government to spend a couple of hundred million dollars on a drug that proves successful, but quite another (at least politically) to spend equivalent amounts on each of several drugs, none of which succeeds.

Other political considerations pose barriers as well. For example, supposing the Canadian government chose to fund clinical trials on DCA as a cancer treatment (see the earlier explanation) and supposing it did prove successful, the knowledge acquired through that trial would, under this system, be a public good and non-excludable *internationally*. Canada would be making a gift of a cancer treatment to the world. This may be laudable, but applied to a large number of drugs, the question arises as to whether trials should be funded solely by the taxpayers of the country in which they are undertaken or whether some mechanism should exist for recovering part of the cost from beneficiaries in other countries. At the very least, countries would be sorely tempted to free-ride or at least to stay away from funding trials of drugs that have a low probability of success. International agreements may address how the cost of successful trials would be shared, but such agreements are not easy to reach and, once again, would only work in the case of successful trials. The DCA case would be particularly troublesome since the drug is in the public domain and could be available as a generic immediately, everywhere in the world. In other cases, would the Canadian government simply patent drugs in the US and act as a profit maximizing monopolist to recover R&D costs from American patients?

In some cases, public funding of clinical trials makes sense.

One feature of the product patent system is that all users of a successful drug contribute to the R&D enterprise through its price. When a company patents a drug in a number of countries and when large-scale re-importation is restricted, the drug can be priced in each country on willingness and ability to pay. In other words, countries contribute to the R&D enterprise to at least some degree proportionally to their income. This is probably a more workable and acceptable mechanism than one instructing the government of Luxembourg that, because its citizens have (by some measures) the highest incomes in the world, they must pay the highest price in the world for a new cancer drug and that they should make their cheques out to the Receiver General of Canada.

In some cases, public funding of clinical trials makes sense, such as those involving drugs for diseases endemic to the poorest countries, or in cases where regulators have decided that certain drugs which had been grandfathered onto the market need to undergo proper evaluation. In the United States,the FDA has offered any company doing such an evaluation a period of market exclusivity, even if the drug was already widely available. The case of the gout drug, Colcrys, made headlines when the company that performed the

evaluation raised the price of the drug from pennies to US$5 a pill.[9] In that case, the government should have paid for the testing and made the results generally available.

Prizes and Buyouts

Suggestions that involve (in one form or another) buying out patents all have fundamental weaknesses.

The idea of offering prizes to develop cures for certain diseases has widespread support, especially since the publicity around the X Prize for manned spaceflight. However, the X Prize did not cover the development expenses of the winning entry nor those of the other entrants, so in the case of pharmaceutical development, some mechanism for making the final drug profitable would still be needed. Prizes also have the drawback that someone has to define the objectives of the contest and set the parameters for winning. Proponents of prizes tend to cite the case of John Harrison and the marine chronometer (Sobel 1996), but it is worth bearing in mind the trouble Harrison had collecting his prize.

The idea of offering prizes to develop cures for certain diseases has widespread support.

Some proposals involve governments buying out patents based on a calculation of the value of the health improvement the drug is expected to produce and putting the drug in the public domain where any manufacturer of generic drugs could produce and sell it. The idea here is that tax revenue would cover the cost of developing the drug so that it was spread over a large segment of the population, while the drug itself would be sold at something close to cost of production.

Most of these proposals rather casually assume that a suitable measure of the value of health improvement exists. They tend to invoke QALYs (Quality Adjusted Life Years), a standard unit of measurement in the literature on cost-effectiveness. Countries that perform such analyses as part of their process of deciding whether, for example, to cover individual drugs under government drug plans generally require pharmaceutical companies to provide these calculations. The UK is moving towards value-based pricing for drugs covered under the National Health Service using QALYs, but in spite of that apparent endorsement, it is easy to overestimate the value of the concept of a QALY. As measures of the value of health improvements, QALYs are not as firmly established as some of the literature would suggest. This approach, in other words, runs the risk of assuming away the really difficult bit. On the other hand, Hollis's Health Impact Fund (HIF) proposal, which would use QALYs to allocate rewards among participating pharmaceutical companies, but leaves the choice of taking payment from the HIF or retaining patent-based monopoly rights up to the individual company would probably encourage research into treatments for the neglected diseases of underdeveloped countries, where the total number of QALYs produced would be large simply because of the numbers of people involved, but the value of a monopoly patent would be small because of the extremely low income of most potential patients.

Auctions for Trial Rights

Another proposal involves the government auctioning the right to conduct clinical trials of drugs under the condition that, should the drug make it to market, any company could manufacture it, but the winner of the auction would receive royalty payments on a per-unit basis at a predetermined rate from each manufacturer. The auction would take the form of bids for that royalty rate and the winner would be the company that placed the lowest bid (quoted the lowest per-unit royalty rate) in return for running the clinical trials.

This proposal is interesting in that it divides the drug industry into three components: pre-clinical research, clinical trials, and manufacturing. Research at the pre-clinical stage would lead to the registering of a patent,

9 See Hobson 2011 and the links therein.

as it does now. The clinical trials stage would be managed by Contractual Research Organizations (CROs) – bodies that run clinical trials under contract to pharmaceutical companies. The manufacturing stage would consist of manufacturers of generic drugs, producing drugs that succeeded at the CRO stage and marketing them in a competitive environment (since all drugs would become generic immediately) with the exception that all manufacturers would pay a common, pre-determined royalty rate to the CRO. The CRO that won the right to run trials and receive royalty payments on a particular drug would be the one that won the auction for those rights by placing the lowest bid for a royalty rate. The risks associated with drug development would not disappear – those risks are inherent in the drug development process – but would be borne by the CRO's shareholders. (At present those risks are borne by the shareholders of the drug companies which run the clinical trials, so the location of the risk-bearing would not change significantly.) Those shareholders would also bear the risk that the winning CRO bid too low a royalty rate: again, this simply tightens the focus on where the risk of drug development rests. An appealing feature of this approach is precisely that the risk of drug development is borne by individuals who voluntarily choose to buy shares in the CRO, not with the tax-paying population as would be true under some proposals. This approach is in some ways a relatively minor extension of certain structural changes that some parts of the drug sector have been experiencing lately, with the pre-clinical research being done by stand-alone research institutes which then effectively auction themselves or their product to research-based drug companies for the clinical stages of the research. Certain details would still have to be resolved – how the first-stage research institutes would be funded (at least to some degree out of the CRO's royalty stream, for example?) and how this system would handle the search for new uses for existing drugs.

It is not always easy to distinguish between productive and unproductive entrepreneurship.

Like others, however, this proposal is liable to run into problems associated with international drug sales. If it were possible to implement a proposal along these lines internationally, the winning bidder would receive a payment from every manufacturer of generic drugs selling a version of the drug anywhere. That situation might simultaneously reduce the winning royalty-rate bid and increase the reward to the company, which makes it attractive. If the proposal could not be implemented internationally, however, it is likely to only be practical in large markets. It is not clear whether royalties from the Canadian market would cover the cost of running a full-scale clinical trial in Canada, especially if the targeted disease only affected a relatively small segment of the population. In that case, the company would have to be compensated for the lost revenue from sales under regular patent pricing procedures in other countries. As well, the location of the trials may have political implications: if Indian pharmaceutical companies, which are developing the capacity to run trials at a significantly lower cost than can be done in North America, were to win auctions on a regular basis, outsourcing this particular research activity would probably be a cause for, at least political, concern.

Patent Reform and the European Union

It is not always easy to distinguish between productive and unproductive entrepreneurship. One of the major stumbling blocks in the current free trade negotiations between Canada and the European Union is disagreement about proposed changes to Canadian intellectual property law as it applies to pharmaceuticals. This paper has argued that pharmaceutical research is driven by retained earnings, and noted Scherer's

evidence that cycles in pharmaceutical research activity follow cycles in pharmaceutical gross profitability. This suggests that anything that increased those earnings, as would happen if Canada agreed to the EU's proposed changes,[10] would increase pharmaceutical research activity, which, in the long run, would be a good thing. On the other hand, there is a powerful suspicion that the ability of the European pharmaceutical sector to get its policy proposals included in the EU's bargaining position is the result of unproductive entrepreneurship playing on the mercantilist leanings of most EU member states. And the tendency to refer to pharmaceutical IP as a stumbling block to an agreement suggests that Canadian pharmaceutical consumers must bear the cost of proposals to improve Canada's access to European markets generally. Anyone supporting the latter position is implying that the IP proposals are bad (from a patent point of view) for Canada, but that the deal itself is worthwhile.

Patent Extensions

The EU proposals cover a number of areas, not all of which are addressed here. At least one proposal has considerable merit: the proposal to grant patent extensions when the administrative and clinical trials processes delay a drug's entry to market. Canadian law does not allow for such extensions.

Compensating for legal delays in patents seems reasonable.

Compensating for the law's delay seems reasonable, not just for drugs whose entry to market is delayed by an unusually long approval process (repeated requests for more data, for example) but for the examination and approval process in general. The caveat one would wish to apply is that the delay to be compensated for must originate from the regulatory side, not from the pharmaceutical side.

Data Exclusivity

The merit of the proposal on data exclusivity is less clear. Data exclusivity is a separate matter from the sort of market exclusivity granted by a patent. Rather, it defines a category of trade secret that might be used to delay the entry of manufacturers of generic drugs. Data exclusivity relates to the requirement that a generic drug be demonstrated to be safe and effective. Brand-name drugs must be supported by evidence of safety and efficacy drawn from clinical trials as part of the process of obtaining market approval. Generics are typically bioequivalent to brand-name drugs, but must also provide some evidence of safety and efficacy. An easy way of providing this evidence is to cite the data in the registration file provided by the company that produced the brand-name version. Data exclusivity prohibits registration data being made available to other companies or being used by regulatory authorities to approve a bioequivalent generic for a certain time. Whether data exclusivity actually extends patent life depends on a range of circumstances. If the period of exclusivity, which begins with marketing approval being granted for a drug, is long enough and the remaining patent life short enough, it might outlast the remaining patent life and delay the entry of generic drugs. Without access to the information in the original registration file, manufacturers of generic drugs would have to run their own clinical trials to provide evidence on safety and efficacy.

Data exclusivity can also be used to cover for weak patents. If a manufacturer of generic drugs successfully challenges a patent, it could enter the market with its own version. Successfully challenging a patent, however, does not grant access to the registration file data for the original drug: the granting of a patent and the granting of data exclusivity are two separate processes and two separate mechanisms for protecting market exclusivity. A manufacturer of generic drugs that successfully challenged a patent might, in the face of sufficient protection for data exclusivity, still not be able to enter the market. At present, Canada provides

10 For a summary and critical assessment of the proposals, see Grootendorst and Hollis 2011.

roughly eight years of data exclusivity for innovative drugs; the EU proposal calls for ten years of data exclusivity for all drugs, not just innovative ones.

As noted above, data exclusivity is a separate process from patent protection. There appears to be no particularly good justification for creating a second mechanism for protecting market position, especially if it were used to re-enforce weak patents, since evidence of drug safety and efficacy should be put into the public domain as early as possible. If it were appropriate to extend a brand-name drug's period of monopoly protection, it is more efficient to do it directly through the patent system.

Data exclusivity might be a useful instrument in one circumstance, however. At present, Canada does not grant data exclusivity for new uses of existing drugs. As stated above, the patent system does not provide an incentive for research-based pharmaceutical companies to investigate new uses of older, especially out-of-patent, drugs because they would incur the costs of clinical trials for the new use, but any manufacturer of generic drugs would be able to market the drug for the new use as soon as approval was granted. It is possible that properly structured data exclusivity laws might reward investigation of new uses for old drugs.

Canada does not grant data exclusivity for new uses of existing drugs.

Right of Appeal and Evergreening

A proposal that deals with the right of appeal tackles the issue of evergreening of drugs. In principle, a Supreme Court ruling (Kondro 2006, p. 1508) in 2006 should have made evergreening difficult, if not impossible in Canada. In practice, an increasing number of drugs are protected by a thicket of patents, all expiring at different times and not all necessarily reflecting significant therapeutic improvements. This sort of tangle serves two purposes: 1) to evergreen the original patent; and 2) to make it more difficult for a manufacturer of generic drugs to enter the market by challenging the original patent's validity before it expires. Even if that challenge were to succeed, a range of other carefully structured patents might still protect the drug.

This seems like an unproductive use of the resources paid to the lawyers who write and defend the patents on the one side, and the lawyers who challenge them on the other. This reflects earlier comments on evergreening that recommend setting the bar for patenting high enough that only significant improvements can be patented, requiring manufacturers of generic drugs to pay a compulsory licence fee to the patent holder, and perhaps defining a fixed period of monopoly protection for any newly patented drug (including compensation for administrative time) that would be very difficult to extend.

As always, there are caveats. Allowing a drug to be patented early in the development stage, then permitting a fixed period of market exclusivity after regulatory approval – no matter how long the clinical trial process took – might lead to a drawn out clinical trial phase that could, in turn, delay the entry of the drugs to market. Some critics might welcome a lengthened clinical trial period on the grounds that the present system encourages companies to rush through trials to maximize the part of the patent protection that translates into a monopoly in a particular market. On the whole, however, it seems desirable to create incentives to move the process along expeditiously, perhaps by encouraging patent competition from other pharmaceutical companies working on the same problem (without violating each other's patents).

Other Changes

The patent system would benefit from changes, but not necessarily, as some have argued, from tightening. Tightening tends to imply making it easier for first entrants to fend off competition, which is not always the way to encourage creative destruction. Changes would include providing clear operational definitions for concepts like novelty and obviousness, than are currently available. Unfortunately, the usual policy response to a statement like "the patent system would benefit from changes" is to add rules and to complicate matters, and usually to do both in a hurry. In the case of drug patents, the incentives in the system need to be reviewed to ensure that they point in the direction of productive entrepreneurship.

For all its flaws, the patent system is probably still the best mechanism for encouraging pharmaceutical R&D.

For all its flaws, the patent system is probably still the best mechanism for encouraging pharmaceutical R&D, at least in the real world where neither companies nor governments are perfect or infallible.

References

Arrowsmith, John, 2011a, News and Analysis. Trial Watch: Phase II failures, 2008-2010. *Nature Reviews Drug Discovery*, Vol. 10 (May), pp. 328-29.

Arrowsmith, John, 2011b, News and Analysis, Trial Watch: Phase III and submission failures: 2007-2010. *Nature Reviews Drug Discovery*, Vol. 10, no. 87 (February).

Baumol, William J., 1990, "Entrepreneurship, Productive, Unproductive and Destructive," *Journal of Political Economy* (October).

Boldrin, Michele, and David K. Levine, 2008, *Against Intellectual Monopoly* (Cambridge University Press). Available at <http://www.dklevine.com/general/intellectual/againstfinal.htm>, accessed December 12, 2011.

Cutler, David M., 2001, "The Demise of the Blockbuster?" *New England Journal of Medicine* (March 29).

DiMasi, Joseph, and Cherie Paquette, 2004, "The Economics of Follow-on Drug Research and Development," *Pharmacoeconomics 22* (Suppl. 2), pp. 1-14.

Hollis, Aidan, 2007, *Incentive Mechanisms for Innovation*, IAPR Technical Paper TP-07005, University of Calgary (June).

Grootendorst, Paul, 2009, *How Should We Support Pharmaceutical Innovation?* SEDAP Research Paper 246, McMaster University (May).

Grootendorst, Paul, and Aiden Hollis, 2011, *The Canada-European Union Comprehensive Economic and Trade Agreement: An Economic Impact Assessment of Proposed Pharmaceutical Intellectual Property Provisions*, study commissioned by the Canadian Generic Pharmaceutical Association (February). Available at <http://individual.utoronto.ca/grootendorst/pdf/02.07.11CETAEconomicImpactAssessment-FinalEnglish.pdf>, accessed December 12, 2011.

Grootendorst, Paul, Aidan Hollis, David K. Levine, Thomas Pogge, and Aled Edwards, 2010, "New Approaches to Rewarding Pharmaceutical Innovation," *Canadian Medical Association Journal* (December 13).

Hobson, Katherine, May 24, 2011, Members of Congress Ask URL Pharma About Gout Drug Price. Health Blog. Wall Street Journal. Available at: <http://blogs.wsj.com/health/2011/05/24/members-of-congress-ask-url-pharma-about-gout-drug-price/>, accessed December 12, 2011.

Jayadev, Arjun, and Joseph Stiglitz, 2008, "Two Ideas to Increase Innovation and Reduce Pharmaceutical Costs and Prices," *Health Affairs Web Exclusive* (December).

Kingston, William, 2000, "Antibiotics, Invention and Innovation," *Research Policy*, Vol. 29.

Kondro, Wayne, 2006, "Supreme Court Rules against Drug Patent 'Evergreening,'" *Canadian Medical Association Journal,* Vol. 175 (December 5).

Kremer, Michael, 1997, *Patent Buy-Outs: A Mechanism for Encouraging Innovation*, National Bureau of Economic Research Working Paper 6304 (December).

Moser, Petra, 2007, *Why Don't Inventors Patent?* National Bureau of Economic Research Working Paper 13294 (August).

Moser, Petra, 2011, Innovation Without Patents – Evidence from the Word Fairs (April 15). Available at SSRN: <http://ssrn.com/abstract=930241>

Nordhaus, William D., 2004, *Schumpeterian Profits in the American Economy: Theory and Measurement*, Cowles Foundation Discussion Paper No. 1457 (Yale University).

Rubenstein, Sarah, September 16, 2008, "Inhaled Insulin Gasps for Breath." Health Blog. *Wall Street Journa*l. <http://blogs.wsj.com/health/2008/09/16/inhaled-insulin-gasps-for-breath/>, accessed December 12, 2011.

Scherer, F.M., 1996, *The Size distribution of Profits from Innovation,* ZEW Discussion Paper 96-13. Zentrum for Europaische Wirtschaftsforschung GmbH.

Scherer, F.M., 2001, "The Link between Gross Profitability and Pharmaceutical R&D Spending," *Health Affair*s, Vol. 20, no. 5 (September), pp. 216-220.

Scherer, F.M., and D. Harhoff, 2000, "Technology Policy for a World of Skew-distributed Outcomes," *Research Policy,* Vol. 29, pp. 559-566.

Scherer, F.M., and S. Weisburst, 1995, "Economic Effects of Strengthening Pharmaceutical Patent Protection in Italy," *International Review of Industrial Property and Copyright Law*, Vol. 26.

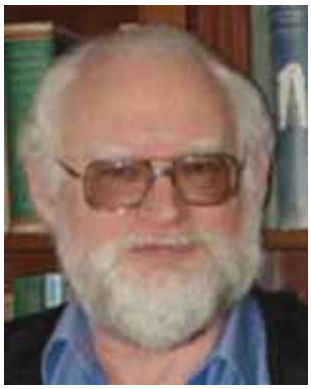
Schumpeter, Joseph, 2008 (orig. pub. 1942), *Capitalism, Socialism and Democracy* (Harper Perennial).

Sobel, Dava, 1996, *Longitude: The True Story of a Lone Genius Who Solved the Greatest Scientific Problem of His Time* (Penguin).

Tabarrok, Alexander, 2002, "Patent Theory and Patent Law," *Contributions to Economic Analysis and Policy*, Vol 1 (Issue 1, Article 9).

Temin, Peter, 1980, *Taking Your Medicine – Drug Regulation in the United States* (Harvard University Press).

About the Author



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Intellectual Property Law and the Pharmaceutical Industry: An Analysis of the Canadian Framework

Kristina M. Lybecker, Ph.D.

Introduction

The unique structure of the innovative pharmaceutical industry necessitates a variety of intellectual property protection mechanisms. Specifically, the industry is characterized by a research and development (R&D) process that is lengthy, expensive, uncertain, and risky. Recent estimates of the cost of developing a new medicine are US$1.3 billion (DiMasi and Grabowski 2007, 469). Moreover, new drug development takes an average of 10 to 15 years with no guarantee of success (PhRMA n.d.). Admittedly, these figures are highly controversial, but pharmaceutical innovation is unquestionably an expensive and lengthy undertaking. Regardless of the extent of overestimation or underestimation of the cost of pharmaceutical research and development, it is a tremendously costly endeavour. Innovation is essential to the industry and the source of both profits and growth. Accordingly, patent protection is disproportionately more important for ensuring that the innovator appropriates the returns to R&D to the pharmaceutical industry than virtually any other. Building on the 1987 "Yale Survey" (Levin, Klevorick, Nelson, and Winter 1987), the "Carnegie Mellon Survey" found that while patents are again seen as "unambiguously the least effective appropriability mechanisms," the drug industry regards them as strictly more effective than alternative mechanisms (Cohen, Richard, and Walsh 1996). The industry's disproportionate reliance on patents and other forms of intellectual property protection is confirmed in numerous other studies.[1]

Protection provided by the patent system provides innovators with the incentive to invest in new technologies.

Fundamentally, the protection provided by the patent system provides innovators with the incentive to invest in new technologies that could otherwise easily be replicated and sold by competing firms. This potential for free riding on the fixed costs borne by the innovating firm constitutes a market failure that would discourage most innovation in the absence of intellectual property protection. Patents and the other forms of intellectual property rights protection address this market failure, providing innovators with a limited period of market exclusivity. Essentially, patents entail an efficiency trade off. Society balances market exclusivity to encourage innovation against public access to this knowledge. In effect, in exchange for granting the

1 These include: Levin, Klevorick, Nelson and Winter (1987), Taylor and Silberston (1973), Scherer (1997), Mansfield (1986), Mansfield, Schwartz and Wagner (1981), and Tocker (1988). These studies are echoed by arguments from within the pharmaceutical industry: Mossinghoff (1998), Peretz (1983), Mossinghoff (1987), Santoro (1995), Smith (1990a, 1990b), Mossinghoff and Bombelles (1996), PhRMA (1997), and Bombelles (1999).

innovator a limited period of market exclusivity, a temporary static loss, society gains complete knowledge of the innovation through disclosure, a permanent dynamic gain. Through this trade off, the existing patent system corrects the market failure that would stymie most innovation.

The legal and economic issues surrounding the pharmaceutical industry are distinct from other innovation-intensive industries due to the presence of three interrelated features. As described by Danzon (1999), these three features are 1) the rapid pace of technological change and the vital importance of intellectual property protection, 2) the regulation of virtually every aspect of the industry, and 3) the global nature of pharmaceutical research and development and incentive for free-riding on the global joint costs of development. Each of these elements poses unique economic and legal challenges in the innovation of new drugs and the public health policies that surround their production and distribution.

Danzon (1999) argues that since the pharmaceutical industry is characterized by an unusually high rate of R&D, intellectual property protection is critically important. This provides for the potential for significant market power and monopoly pricing, which raises numerous public health policy questions surrounding prices and profits. Moreover, she notes that virtually every aspect of the industry is heavily regulated, from safety and efficacy, to promotion and advertising, to pricing and reimbursement. The impact of these regulations are "profound and multidimensional even within a single country, affecting consumption patterns, productivity, R&D and hence the supply of future technologies" (Danzon 1999, 1056). Finally, pharmaceutical research and development is a global public good though the research costs are borne solely by the innovator firm. "Each country faces an incentive to adopt the regulatory policies that best control its pharmaceutical budget in the short run, free-riding on others to pay for the joint costs of R&D and ignoring cross-national spillovers of national regulatory policies through parallel trade and international price comparisons" (Danzon 1999, 1056).

In exchange for granting the innovator a limited period of market exclusivity, society gains complete knowledge of the innovation through disclosure,

Without question, the legal framework surrounding intellectual property protection and the national regulatory regime are powerful forces shaping the pharmaceutical industry, its profitability, productivity, and innovative future. This paper examines the legal frameworks surrounding intellectual property in the pharmaceutical industry across a variety of countries. This analysis is done to determine best practices and describe the legal environment that will most effectively foster a robust, innovative pharmaceutical industry. The paper considers the Canadian regime by exploring the objectives of a strong legal framework and makes recommendations to further strengthen the legal architecture surrounding pharmaceutical intellectual property in Canada.

Legal Frameworks for Intellectual Property in the Pharmaceutical Industry

In cross-country comparisons of patent regimes, it is most useful to examine both the most innovative nations and the emerging markets that show the greatest promise for future innovation. Assuming that greater research and development spending fosters increased innovation and proxies for an innovation-friendly legal regime, the nations with the greatest R&D expenditures possess the legal frameworks most worth examining.

In order to identify the nations garnering the greatest share of research and development dollars, Table 1 presents the figures for research and development spending by geographic region for PhRMA (Pharmaceutical Research and Manufacturers of America) member companies in 2009. It is worth noting that of the top 15 global pharmaceutical corporations in 2009 (listed in Table 2), 13 were PhRMA member companies. Only Roche and Teva were not.

Table 1: R&D spending by Geographic Region by PhRMA member companies, 2009

Geographic Area	Dollars (US millions)	Share
United States	$35,356.0	76.10%
Europe	$8,558.4	18.60%
United Kingdom	$1,937.4	4.20%
Germany	$583.2	1.30%
France	$365.1	0.80%
Italy	$210.5	0.50%
Spain	$223.6	0.50%
Other Western Europe	$4,315.6	9.30%
Japan	$676.2	1.50%
Canada	$444.4	1.00%
Australia & New Zealand	$181.7	0.40%
China	$124.4	0.30%
India	$125.1	0.30%
Middle East	$120.7	0.30%
Brazil	$100.9	0.20%
Africa	$43.1	0.10%
South Korea	$32.4	0.06%
Total R&D	$46,441.6	

Source: PhRMA Industry Profile 2011, 46.
Note: All figures include company-financed R&D only. Total values may be affected by rounding.

Table 2: Top 15 Global Pharmaceutical Corporations, 2009

	Corporation
1	Pfizer
2	Merck & Co.
3	Novartis
4	Sanofi-Aventis
5	Glaxosmithkline
6	Astrazeneca
7	Roche
8	Johnson & Johnson
9	Eli Lilly
10	Abbott
11	Teva
12	Bayer
13	Boehringer Ingel
14	Amgen
15	Takeda

Source: IMAP Healthcare 2011, 11.

The highest levels of research and development spending done by PhRMA member companies, as described in Table 1, include the United States, several Western European nations, and Japan. Accordingly, these are the legal environments most worth exploring. Table 3, below, describes the legal regimes across seven regions: Canada, the United States, the European Union, South Korea, Japan, Australia, and Brazil. The table outlines 16 protection-related issues and describes the national status of each issue by country. Appendix 1 gives a more detailed description of each issue and its importance.

The most significant differences across regimes appear to be in the areas of Patent Term Extensions (where Canada is an outlier without legislation), Price Regulation of Patented Drugs (where the United States is an

outlier without legislation), and Basic Patent Linkage with Automatic Injunction (where Canada, the United States, and Australia have provisions in place while the European Union, South Korea, and Japan do not).[2] The table provides perspective on how different regimes compare and contrast with one another and how Canada measures up across each type of legislation.

Table 3: Comparative Chart of Patent Regimes (See Appendix 1 for definitions of each issue)

	Canada	USA	EU	South Korea	Japan	Australia	Brazil
Basic Patent Term	20	20	20	20	20	20	20
Entitlement to Patent	First to file	First to file (as of March 16, 2013)	First to file	First to file	First to file	First to file	First to file
Patent Term Restoration	No	Yes, 5 years (to a maximum of 14 years)	Yes, 5 years (to a maximum of 15 years)	Yes, 5 years, rarely granted	Yes, 5 years	Yes, 5 years	No
Data Exclusivity	8 years, plus 6 months for pediatric uses	5 years; 3 more years for a new clinical indication	10 years	4-6 years	4-10 years	5 years	Yes, no limit specified
Early-Working Exception	Yes (without stockpiling)	Yes (known in the US as the Bolar Provision)	Yes, since 2007	Yes	Yes	Yes	No
Basic Patent Linkage with Automatic Injunction	Yes, PMNOC	Yes, Hatch-Waxman	No (unnecessary due to the availability of injunctive relief)	No	No	Yes	No
Compulsory Licenses (General)	Yes, never used	Yes, compensa-tion based. Also as antitrust remedy.	No	Yes, if invention is not practiced for more than 3 consecutive years	Yes, if "particularly necessary for the public interest"	Yes	Yes
Compulsory Licenses (Doha Public Health)	Yes	No	Yes	Yes, for emergencies or extremely urgent situations	Yes	No	Yes
Price Regulation of Patented Drugs	Yes	No	Yes	Yes	Yes	Yes	Yes
Interlocutory Injunction in Patent Infringement Court Cases	Possible but rarely awarded	Common in the past. After 2006, a more stringent test results in fewer injunctions.	Varies	Yes	Yes	Yes	Yes

2 It is worth noting that the European Union does not require a "linkage" type regulation due to the availability of injunctive relief within its legal system.

	Canada	USA	EU	South Korea	Japan	Australia	Brazil
Treble Damages for Willful Infringement	No	Yes (but after 2006 a more stringent test applies; treble damages now awarded only in "exceptional cases").	No	No	No	No	No
Sequence Patents	Yes	Yes	Yes	Yes	Yes	Yes	Yes, but only if modified
Unusual Subject Matter Restorations	No	No	Yes, inventions contrary to public order/ morality. Plant and animal varieties.	Yes, isolated parts of human beings, traditional knowledge, inventions contrary to morality/ public order.	Yes, inventions contrary to morality/ public order.	No	Yes, all drug patents must be approved by Ministry of Health. Living beings, in whole or in part, are not patentable.
Post-Grant Challenge to a Patent (Administrative)	Very restricted, rarely used by challengers	Yes, re-examination	Yes, opposition	No, court only	No, court only	Yes, re-examination	Yes, opposition
Mandatory Disclosure of Source and Origin for Genetic Resources and Traditional Knowledge	No	No	Proposed	No	No	No	Yes
Biosimilars/ Subsequent Entry Biologics (SEB) Approval Framework	Yes	Proposed	Yes	Yes	No	Yes	Yes

Source: Foreign Affairs and International Trade Canada, "Comparative Chart of Patent Regimes," May 2009.

Best Practices for Fostering a Robust Innovation-Based Pharmaceutical Industry

Given that patents and other forms of intellectual property protection are disproportionally important to the pharmaceutical industry, the legal architecture required to foster a robust innovation-based industry will be multifaceted. This section aims to set out the objectives of that legal regime and evaluate the characteristics of the legal framework that will best encourage industry growth.

Economic and Efficiency Objectives of the Legislation Surrounding Pharmaceutical IP

From an economic perspective, many factors encourage innovation. The intellectual property rights protection regime surrounding pharmaceutical innovation should reflect these factors and incorporate the elements that both foster future advances and protect existing innovation. The optimal legal regime should promote economic efficiency and enhance social welfare, increasing both consumer and producer surpluses. The below paragraphs describe many of the factors that encourage innovation and safeguard the returns that encourage pharmaceutical research and development. Any new legislation or changes to existing legislation should take these factors into account.

PRESERVATION OF THE INCENTIVES TO INNOVATE

The essence of intellectual property protection is the encouragement of innovation. Economists and legal scholars debate the optimal trade-off between patent length (in years) and breadth (in scope) (Scotchmer 1999; Gilbert and Shapiro 1990). While the treatment of those questions is beyond the scope of this work, it is worth noting that the optimal patent term may differ across countries and across technologies (Danzon 1999, 1066). Although flawed, the existing patent system effectively encourages innovation and has successfully rewarded inventors with returns to their innovations, encouraging a continued stream of new technologies and advances. The system balances the dynamic gains from innovation disclosure against the static losses from monopoly profits, bringing new therapies to patients and rewarding firms for the risk and investment inherent in the R&D process.

The essence of intellectual property protection is the encouragement of innovation.

CONTINUED COMMITMENTS TO SAFETY AND EFFICACY

Any changes in legislation should preserve the existing system's commitment to safety and efficacy, ensuring the health of the patient above all. While more rapid review times increase firm profitability, these incentives should not come at the cost of assured safety.

INCREASED R&D ON ORPHAN DRUGS AND TREATMENTS FOR NEGLECTED DISEASES WITH HIGH SOCIAL VALUE

Unfortunately, the existing patent system fails to provide incentives for research into orphan (rare) diseases and diseases of the poor due to a lack of profits. As there is no official Canadian definition of rare diseases, it is worth looking to other nations for statistical perspective on these conditions. In the United States, rare diseases are those affecting fewer than 200,000 Americans, while the European Union defines such diseases as those affecting 1 per 2,000 or fewer people. Overcoming this obstacle to drug development for these types of diseases would enhance global social welfare and provide the potential for therapeutic relief to many of the world's most vulnerable.

MECHANISMS FOR REWARDING INCREMENTAL INNOVATION

While it may be argued that incremental innovations will contribute less to social welfare than innovations that are both first-in-class and best-in-class, follow-on innovations are nonetheless important advances and worth encouraging. Optimal patent regimes will reward subsequent innovations and also allow original innovators to capture a share of the returns from incremental innovations that were spurred by the initial technological advance. In this context, critics point to "patent evergreening" as a strategy to obtain multiple patents on the same product, essentially extending the term of exclusivity presented in the original patent grant. At the same time, others note that effective intellectual property protection provides innovators with patents on improvement inventions. A recent study by the Congressional Research Service notes that since much technological innovation occurs incrementally, incremental innovations may provide significant benefit to patients and promote competition (Thomas 2009, ii).

REDUCTION OF EXCESSIVE MARKETING

Excessive marketing expenditures within the pharmaceutical industry are frequently cited by critics as a significant contributor to high drug prices. Ideally, regulations could induce or mandate firms to reduce this spending, in essence de-linking profitability and marketing efforts. The elimination of these costs would reduce drug costs and should help to lower prices.

REDUCED LAUNCH TIMES

Due to differences in national laws and the differential pricing strategies that international pharmaceutical firms employ, drugs are sold at a premium in some countries and for less money in others. Because of this, firms have an incentive to launch new products in the most profitable nations first, those characterized by stronger patent protection and higher prices. Reduced launch times allow innovative treatments to reach patients sooner and sales revenues to accrue to the innovator more quickly.

Pharmaceutical counterfeiting both reduces the incentives for innovation and endangers public health and safety.

REDUCED DUPLICATIVE RESEARCH AND DEVELOPMENT OF "ME TOO" DRUGS

In many cases, national patent systems and the resultant monopoly prices encourage innovators to dedicate R&D efforts to drugs that are unique enough for a patent award, but may provide little or no therapeutic advance. "Me too" drugs are those that are structurally very similar to already known drugs, with only minor differences. They are associated with inefficiency since they drain limited R&D resources for duplicative purposes without providing therapeutic advancements. "According to the US Food and Drug Administration, over 77% of the drugs approved from 1990-2004 were duplicative rather than breakthrough drugs" (Ravvin 2008, p.112, citing a 2005 report by the US Food and Drug Administration). Although these investments do provide the innovating firm with a return, such duplicative research efforts are an inefficient use of scarce research talent and financial resources. A superior legal regime would provide greater incentives for breakthrough therapies and reduce the incentives for "me too" drugs.

PROTECTION AGAINST PHARMACEUTICAL COUNTERFEITING

Pharmaceutical counterfeiting both reduces the incentives for innovation and endangers public health and safety. Fraudulent medicines divert potential sales from innovator companies to criminal enterprises and expose the originator companies to legal liability. An effective intellectual property protection framework will include legislation mandating significant criminal sanctions for pharmaceutical counterfeiting. As outlined by the European Federation of Pharmaceutical Industries and Associations (2010), legislation should prevent pharmaceutical products with false identities, histories, or sources from entering the legal supply chain.

At first blush, the critical importance of patent protection to the pharmaceutical industry seems to suggest that further strengthening IP protection would lead to continually greater innovation. However, recent research seems to refute this conclusion, though a definitive answer remains elusive. Qian (2007) studies whether the implementation of pharmaceutical patents stimulates domestic pharmaceutical R&D expenditures and innovations. Using US patent awards as a measure of innovative activity, Qian finds that national pharmaceutical patent protection alone does not stimulate domestic innovation. Further, she finds that globally, such innovation accelerates with higher levels of economic development, educational attainment, and economic freedom. Most importantly, Qian's study points to an optimal level of intellectual property rights protection, above which greater regulation reduces innovative activities.

These results contrast somewhat with Pazderka's 1999 study on Canadian pharmaceutical innovation. Following the restoration of full patent protection in Canada, Pazderka considers R&D spending trends within the pharmaceutical industry as well as trends in Canada's share of foreign R&D spending of US-owned multinationals. He finds a statistically significant increase in Canadian pharmaceutical R&D spending after 1987 when Bill C-22 was enacted. Nevertheless, he does note the difficulty of establishing the direction of causality between R&D spending and enhanced protection.

The Lanjouw and Cockburn (2001) study provides additional perspective. It examines the link between the extension of pharmaceutical patent protection across the developing world and research on drugs to address the needs of developing countries. Drawing on survey data from India, the authors find some evidence of an initial increase in R&D on diseases endemic to developing nations following legislation protecting pharmaceutical IP.

Overall, the empirical evidence suggests that stronger intellectual property protection for pharmaceuticals stimulates additional investment in R&D and innovation. The preponderance of studies examine patent protection, thus less is understood about the importance of other types of protection and the elements that should characterize other legislation. While IP protection is clearly an essential national strategy, it is crucial to recognize that the pharmaceutical industry is global in nature and laws in one country may affect the health of the industry in another. Danzon (1999) notes that through parallel trade the weak patent protection in one nation "effectively spills over to other countries, undermining the ability of the manufacturer to realize the value of the patent in countries that respect patents" (Danzon 1999, 1068).

Empirical evidence suggests that stronger intellectual property protection for pharmaceuticals stimulates additional investment in R&D and innovation.

Canadian Legal Framework for Pharmaceutical Intellectual Property

In Canada, the legal framework surrounding pharmaceutical intellectual property relies on three legal components. The primary intellectual property law enacted by the federal government is the *Patent Act* (R.S.C., 1985, c.P-4). In addition, two pieces of legislation address the implementation of the regulations: the *Patented Medicines (Notice of Compliance) Regulations* (SOR/93-133) and "Data Protection" found in Canada's *Food and Drug Regulations* (C.R.C., c.870). In addition, Canada is a signatory to a multilateral treaty that addresses intellectual property protection for the pharmaceutical industry: The Agreement on Trade-Related Aspects of Intellectual Property Rights (or the TRIPS Agreement). Canada is also a signatory to a regional economic integration treaty, the North American Free Trade Agreement (NAFTA), parts of which also address intellectual property protection for the pharmaceutical industry.[3]

Following nearly 20 years of compulsory licensing of prescription drugs, Canada repealed the 1969 amendments to the *Patent Act*, restoring full patent protection to pharmaceutical drugs with two legislative changes made in 1987 and 1992. The negotiations over the Free Trade Agreement (FTA) between Canada and the United States resulted in the amendments to the *Patent Act* contained in Bill C-22, which entered into effect on December 7, 1987. Bill C-22 guaranteed patent owners a period of protection from compulsory

3 An excellent description of relevant pieces of legislation and the chronology of significant events may be found in Smith (2000).

licensing for ten years in the case of license to import and seven years (if the chemical was sourced in Canada) in the case of license to manufacture, from the date of the first Notice of Compliance after June 27, 1986. Bill C-22 also provided for a patent term of 20 years from the date of application, as of 1989.

The *Patent Act* was further modified in 1992 under Bill C-91 in order to implement the provisions on intellectual property contained in the TRIPS provisions. Bill C-91 eliminated compulsory licenses for pharmaceutical products, with exceptions for such licenses in existence before the Act came into force. Bill C-91 provides for product patents for pharmaceutical innovations in addition to the process patents that were already available. The bill does include an "early working" exception and a "stockpiling" exemption. Under the early working exemption, a "generic drug manufacturer could develop a generic version of a medicine and take whatever steps were necessary to meet the regulatory requirements pertaining to its sale before the expiry of the relevant patents" (section 55.2(1)) (Smith 2000).

Patents for pharmaceutical products and processes provide for 20 years of exclusivity for an invention disclosed in the patent application.

The protection provided to the pharmaceutical industry by these three key legal regimes play out in three important areas: patents, patent linkage, and data exclusivity. It is worth briefly describing the status of each.

Patents

Patents for pharmaceutical products and processes provide for 20 years of exclusivity for an invention disclosed in the patent application. The criteria for the invention are such that it must be novel, useful, and non-obvious. Given the complexity of pharmaceutical innovation it is common for a single drug to embody many technologies and be protected by many patents with distinct expiry dates.

Patent Linkage

The patent linkage regulations connect the regulatory approval of generic drugs and patents. Prior to bringing a generic drug to market, the generic manufacturer must address the patents asserted to be relevant by the innovator company before Health Canada will issue marketing authorization. The generic firm may await expiry, or claim the relevant patent is invalid or not infringed. The result is that generic firms may first face a summary proceeding to determine patent validity and later risk litigation if infringement is claimed. In like manner, the innovating firm may face litigation under the *NOC Regulations* and also in defending a patent's validity. Through the patent linkage, the *NOC Regulations* seek to balance the incentives for innovation and the timely arrival of generic competition to the market.

Data Exclusivity

As described by Grootendorst and Hollis (2011), innovative drugs are protected from generic competition by Canadian law for a period of eight years through the protection of innovator data. Specifically, the "Minister of Health cannot grant a market authorization to a product that would directly or indirectly rely on the clinical trials sponsored by the firm that obtained the regulatory approval" (Grootendorst and Hollis 2011, 8). This exclusivity does not apply to new indications for existing drugs and only applies to drugs meeting specific criteria, specifically the first chemical entity launched in Canada.

Recommendations

The discussion presented here examined the legal architecture required for more effective intellectual property protection for the innovative pharmaceutical industry. Given the critical importance of patents and other IP protection to this industry, a strong legal regime is key to the development and growth of a robust innovation-based pharmaceutical industry. Several recommendations for Canadian legislation emerge from a consideration of the legal frameworks surrounding intellectual property in the pharmaceutical industry as well as the optimal provisions for such protection.

The appropriate legal framework will depend on the type of industry that one hopes to foster. Clearly the legislation that facilitates the growth of a prospering generic industry differs from that which nurtures a robust innovation-based industry. For example, the compulsory licensing provisions contained in the 1969 amendments to the *Patent Act* contributed in a significant way to the growth of the Canadian generic drug industry (Pazderka 1999, 29). In like manner, Grootendorst and Hollis (2011) predict differential impacts of changes in exclusivity periods across the branded and generic pharmaceutical industries.

Canada is one of the few industrialized nations lacking a policy for rare diseases.

Orphan Drug Legislation

Canada is one of the few industrialized nations lacking a policy for rare diseases. Legislation designed to encourage the development of treatments for rare diseases was passed in the United States in 1983, introduced in Japan in 1993, in Australia in 1997, and in the European Union in 1999. Appropriate legislation would define a rare disease and encourage Canadian firms to intensify their research and develop new therapies. This process could include a specifically designed approach for the review and approval of treatments for rare disorders. It is important to recognize that Canadian firms are already researching rare conditions and new legislation would foster growth in this critical sector. More than 35 Canadian companies have received US Food and Drug Administration Orphan Product designation for their innovations (BIOTECanada n.d.(b)). In the 25 years since the passage of the US Orphan Drug Act, an estimated 280 new therapies have been developed for the US market, benefiting more than 14 million patients (BIOTECanada n.d.(a)). This contrasts with the 10 orphan drug therapies developed prior to the passage of the Act (BIOTECanada n.d.(a)). As described by BIOTECanada, "there are strong correlations between the presence of orphan drug regulations and drug innovation by pharmaceutical and biotech companies and this is mainly attributed to the incentives contained within those regulations to encourage sponsors of Orphan medicinal products to continue to engage in research and development that finds cures for rare diseases" (BIOTECanada n.d.(a)).

Data Exclusivity

In Canada, while innovative drugs are protected from generic competition through the protection of innovator data for eight years, only drugs meeting certain criteria are eligible. In addition, data exclusivity currently does not apply to new uses for existing drugs in Canada. Admittedly, data exclusivity regimes differ across countries in nature, scope, and extent of protection. As described by Grootendorst and Hollis (2011), in the European Union, Directive 2004/27/EC provides for data exclusivity extensions of 8+2+1 years. The United States provides 5 years of data exclusivity with eligibility for an additional three years for exclusivity limited to new and essential clinical trials. In addition, the United States provides 12 years of data exclusivity for new biologics.

This paper recommends language that provides for more expansive data exclusivity protection, such that new uses, not just "innovative drugs" are eligible for protection. Beyond such protection for small-molecule drugs, additional protection should be provided for biologics. The justification for strengthening data exclusivity laws rests in the incentives provided to innovative firms to produce the data required for regulatory approval. "The pharmaceutical and agrochemical industries have often successfully argued that if regulators allow an equivalent product (a "generic") to go to market on the strength of the test data provided by the originator company, there would be no incentive for anyone to produce the test data necessary to obtain market approval" (Krattinger et al. 2007).

Data exclusivity should cover new uses as well as innovative drugs.

Patent Term Extension

An examination of the patent term restoration provisions described in Table 3 reveals that, unlike most other nations, Canada fails to provide an extra period of patent protection as compensation for time lost due to regulatory approval delays. While Canadian law provides for a 20-year patent term, standard under the TRIPS Agreement, there is no provision for the reduction in effective patent life due to the lapse between the filing of a patent and the grant of market authorization. This is an area where Canada differs significantly from the United States and the European Union. In the United States, the 1984 Patent Term Restoration and Competition Act provides innovator companies with one patent term extension per product. Moreover, the firm has the discretion to determine on which patent the extension is sought. Similarly, patent term extensions are available in the European Union for new products. Admittedly, in the United States the 1984 Act provides for expedited post-patent entry by generic manufactures.

Canada fails to provide extra patent protection for time lost due to regulatory delays.

This paper recommends legislation granting a potential patent term extension to innovator firms in order to recoup the time spent attaining regulatory and marketing approval. The restoration of zero to five years, as is the practice in other jurisdictions, would lengthen the effective patent life of innovative therapies, increasing the incentives to invest in the research and development costs that these treatments require.

Anti-counterfeiting Legislation

Finally, this paper recommends that Canada strengthen its anti-counterfeiting legislation. Criminal sanctions in concert with regulatory provisions will safeguard the health of patients and protect the pharmaceutical industry from the threat of fraudulent medicines. Recently the Council of Europe adopted the "Medicrime" Convention on pharmaceutical counterfeiting and similar crimes involving threats to public health. The legislation aims to strengthen product protection measures, ensure reliability in the wholesale distribution of pharmaceuticals, and define clear obligations for starting materials (EFPIA 2010, 3).[4] The World Health Organization's IMPACT Programme echoes these recommendations. Suggestions included in the IMPACT Handbook (2011) include combatting internet distribution of counterfeit pharmaceuticals, establishing guidelines for a rapid response plan, developing good security practices for packaging materials, developing pharmacovigilance systems, and identifying regulatory and legislative gaps (IMPACT Handbook 2011, 34-37).

Canada needs to strengthen its anti-counterfeiting legislation.

4 The EFPIA White Paper cited here provides a comprehensive list of the elements that effective legislation should incorporate.

It is worth noting that the Max Planck Institute in Germany is currently conducting a "Comparative Law Study." The project, which began in 2005 and is expected to be completed later this year, is a comparative study of 12 legal systems worldwide. The study examines the "various methods by which affected countries seek to protect the pharmaceutical sector from counterfeit products and how they counter offenses committed by increasingly internationally-operating offenders."[5] The project focuses on the contributions that criminal law may make to the prevention of pharmaceutical counterfeiting and the evaluation of the efficacy of diverse legal measures.

Conclusions

The pharmaceutical industry is characterized by a research and development process that is lengthy, expensive, uncertain, and risky. Accordingly, relative to other industries, pharmaceutical firms rely disproportionately on patents and other forms of intellectual property protection to ensure innovators are able to appropriate the returns to R&D. Pharmaceutical patents protect process and product innovations and have led to therapies that have enhanced and extended lives on a global scale. This innovation requires protection and this protection requires a trade off. Patents provide that protection; they ensure market exclusivity in exchange for continued investment in innovation.

Reform recommendations provide for an enhanced legal environment to foster a robust, innovative pharmaceutical industry in Canada.

While patent protection for both pharmaceutical products and processes has become the global norm, significant differences exist across national legal frameworks for the protection of pharmaceutical intellectual property. The analysis of the differences across seven regions highlights the differences in IP protection, notably in patent term extensions, orphan product provisions, and data exclusivity legislation. Although each of the legal environments considered complies with WTO obligations and other multinational conventions, it is possible to distinguish where protection most advances a vigorous, innovation-based pharmaceutical industry.

This study provides an analysis of the best practices in pharmaceutical intellectual property protection and describes the optimal legal architecture. It then defines and compares Canada's legal framework to that of other regimes, resulting in several recommendations for potential changes to the Canadian system. Recognizing that the recommendations will have different effects on the innovation-based and generic pharmaceutical industries, the suggestions provide for an enhanced legal environment to foster a robust, innovative pharmaceutical industry.

5 Additional information about the Max Planck Institute Comparative Law Study may be found at: <http://www.mpicc.de/ww/en/pub/forschung/forschungsarbeit/strafrecht/pharmaceutical_counterfeiting.htm>

References

BIOTECanada, n.d.(a), *BIOTECanada Legislative Proposals to Create a National Orphan Product Policy*, online posting. Available at: <http://www.biotech.ca/uploads/btc%20leg%20proposals.pdf>, accessed November 11, 2011.

BIOTECanada, n.d (b), *Rare Disease Treatment in Canada: Need for a National Orphan Product Policy*, online posting. Available at: <http://www.biotech.ca/uploads/rare%20dieases%20issue%20brief%202010.pdf>, accessed November 11, 2011.

Canada. *Patent Act* (R.S.C., 1985, c. P-4). World Intellectual Property Organization (WIPO) Collection of Laws for Electronic Access (CLEA) database. <http://www.wipo.int/wipolex/en/text.jsp?file_id=207521>, accessed November 3, 2011.

Canada. *Patented Medicines (Notice of Compliance) Regulations* (SOR/93-133). World Intellectual Property Organization (WIPO) Collection of Laws for Electronic Access (CLEA) database. <http://www.wipo.int/wipolex/en/text.jsp?file_id=222609>, accessed November 3, 2011.

Canada. *Food and Drug Regulations* (C.R.C., c. 970). World Intellectual Property Organization (WIPO) Collection of Laws for Electronic Access (CLEA) database. <http://www.wipo.int/wipolex/en/text.jsp?file_id=220594>, accessed November 3, 2011.

Chaudhuri, Shubham, Pinelopi K. Goldberg, and Panle Jia, 2006, "Estimating the Effects of Global Patent Protection in Pharmaceuticals: A Case Study of Quinolones in India," *The American Economic Review*, vol. 96, no. 5 (December), pp. 1477-1514.

Cohen W.M., R.N. Nelson, and J. Walsh, 1996, *A first look at the results of the 1994 Carnegie Mellon Survey of Industrial R&D in the United States*, Unpublished manuscript (February 28).

Danzon, Patricia M., 1999, "The Pharmaceutical Industry," in Boudewijn Bouckaert and Gerrit De Gees (eds.), *5880 The Encyclopedia of Law and Economics*, pp. 1055-1091. Available at: <http://encyclo.findlaw.com/5880book.pdf>, accessed November 3, 2011.

DiMasi, J.A., and H.G. Grabowski, 2007, "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics*, vol. 28, pp. 469-479.

European Federation of Pharmaceutical Industries and Associations (EFPIA). "White Paper on The Anti-Counterfeiting of Medicines," EFPIA Anti-Counterfeiting Group, online post, November 2, 2010. Available at: <http://www.efpia.eu/Content/Default.asp?PageID=559&DocID=10187>, accessed November 11, 2011.

Faunce, Thomas A., and Joel Lexchin, 2007, "'Linkage' Pharmaceutical Evergreening in Canada and Australia," *Australia and New Zealand Health Policy*, vol. 4. Available at: <http://www.anzhealthpolicy.com/content/4/1/8>, accessed November 2, 2011.

Gilbert, Richard, and Carl Shapiro, 1990, "Optimal Patent Length and Breadth," *The RAND Journal of Economics*, vol. 21, no. 1 (Spring), pp.106-112.

Grootendorst, Paul, and Aidan Hollis, 2011, "The Canada-European Union Comprehensive Economic and Trade Agreement: An Economic Impact Assessment of Proposed Pharmaceutical Intellectual Property Provisions," working paper commissioned by the Canadian Generic Pharmaceutical Association (February 7). Available online at: <http://individual.utoronto.ca/grootendorst/pdf/02.07.11CETAEconomicImpactAssessment-FinalEnglish.pdf>, accessed November 2, 2011.

IMAP Healthcare, "Pharmaceutical and Biotech Industry Global Report—2011," IMAP, web posting. Available at: <http://www.imap.com/imap/media/resources/IMAP_PharmaReport_8_272B8752E0FB3.pdf>, accessed on November 5, 2011.

IMS Health, 2010, "IMS Health Forecasts Global Pharmaceutical Market Growth of 5-7 Percent in 2011, Reaching $880 Billion," press release (October 6). Available at: <http://www.imshealth.com/portal/site/imshealth/menuitem.a46c6d4df3db4b3d88f611019418c22a/?vgnextoid=119717f27128b210VgnVCM100000ed152ca2RCRD>, accessed November 3, 2011.

Klemperer, Paul, 1990, "How Broad Should the Scope of Patent Protection Be?" T*he RAND Journal of Economics*, vol. 21, no. 1 (Spring), pp.113-130.

Krattiger A., R.T. Mahoney, L. Nelsen, J.A. Thomson, A.B. Bennett, K. Satyanarayana, G.D. Graff, C. Fernandez, and S.P. Kowalski, 2007, "Editor's Summary: Implications and Best Practices," Chapter 4.9 and 4.10, *Intellectual Property Management in Health and Agricultural Innovation: A Handbook of Best Practices* (MIHR: Oxford, U.K. and PIPRA: Davis, U.S.A.). Available online at <www.ipHandbook.org>, accessed November 11, 2011.

Lanjouw, Jean O., and Iain M. Cockburn, 2001, "New Pills for Poor People? Empirical Evidence after GATT," *World Development*, vol. 29, no. 2 (February), pp. 265-289.

Levin, R.C., A.K. Klevorick, R.R. Nelson, and S.G. Winter, 1987, "Appropriating the Returns from Industrial Research and Development," *Brookings Papers on Economic Activity*, (Special Issue), no. 3, pp. 783-831.

Lybecker, Kristina M., and Robert A. Freeman, 2007, "Funding Pharmaceutical Innovation through Direct Tax Credits," *Health Economics, Policy and Law*, vol. 2, pp. 267–284.

Mansfield, Edwin, 1986, "Patents and Innovations: An Empirical Study," *Management Science*, vol. 32, no. 2 (February), pp. 173-181.

Mansfield, Edwin, Mark Schwartz, and Sam Wagner, 1981, "Imitation Costs and Patents: An Empirical Study," *Economic Journal*, vol. 91, no. 364 (December), pp. 907-918.

Mossinghoff, Gerald J., 1998, "Encouraging Invention and Innovation: The Key to Human Progress," PhRMA: Pharmaceutical Research and Manufacturers of America, online posting (January).

Mossinghoff, Gerald J., and Thomas Bombelles, 1996, "The Importance of Intellectual Property Protection to the American Research-Intensive Pharmaceutical Industry," *Columbia Journal of World Business*, vol. XXXI, no. 1 (Spring), pp. 38-48.

Mossinghoff, Gerald J., 1987, "Research-Based Pharmaceutical Companies: The Need for Improved Patent Protection Worldwide," *Journal of Law and Technology*, vol. 2, no. 2, pp. 307-324.

O'Donoghue, Ted, 1998, "A Patentability Requirement for Sequential Innovation," *The RAND Journal of Economics*, vol. 29, no. 4 (Winter), pp. 654-679.

Pazderka, Bohumír, 1999, "Patent Protection and Pharmaceutical R&D Spending in Canada," *Canadian Public Policy / Analyse de Politiques*, vol. 25, no. 1 (March), pp. 29-46.

Peretz, S. Michael, 1983, "Pharmaceuticals in the Third World: The Problem from the Suppliers' Point of View," *World Development*, vol. 11, no. 3 (March), pp.259-264.

Pharmaceutical Research and Manufacturers of America (PhRMA), n.d., "The Research and Development Process," online posting. Available at: <http://www.phrma.org/research-development-process>, accessed October 15, 2011.

Qian, Yi, 2007, "Do National Patent Laws Stimulate Domestic Innovation in a Global Patenting Environment? A Cross-Country Analysis of Pharmaceutical Patent Protection, 1978-2002," *Review of Economics and Statistics*, vol. 89, no. 3 (August), pp. 436-453.

Ravvin, Michael, 2008, "Incentivizing Access and Innovation for Essential Medicines: A Survey of the Problem and Proposed Solutions," *Public Health Economics*, vol. 1, no. 2, pp. 110-123.

Santoro, Michael, 1995, "Pfizer: Global Protection of Intellectual Property," Harvard Business School Case Study N9-392-073 (April 6).

Scherer, F.M., 1997, *The Economic Effect of Compulsory Patent Licensing*, Monograph Series in Finance and Economics (New York, NY: New York University).

Scotchmer, Suzanne, 1999, "On the Optimality of the Patent Renewal System," T*he RAND Journal of Economics*, vol. 30, no. 2 (Summer), pp. 181-196.

Scotchmer, Suzanne, 1991, "Standing on the Shoulders of Giants: Cumulative Research and the Patent Law," *The Journal of Economic Perspectives*, vol. 5, no. 1 (Winter), pp. 29-41.

Smith, Margaret, 2000, "Patent Protection for Pharmaceutical Products in Canada—Chronology of Significant Events," Government of Canada, PRB 99-46E, online posting. Available at: <http://dsp-psd.pwgsc.gc.ca/Collection-R/LoPBdP/BP/prb9946-e.htm>, accessed November 10, 2011.

Smith, N. Craig, 1990, "Note on Pharmaceutical Marketing Practices in the Third World," Harvard Business School Case Study N9-590-032 (December 16).

Smith, N. Craig, 1990, "Ciba-Geigy Pharmaceuticals: Pharma International," Harvard Business School Case Study N9-589-108 (December 14).

Taylor, C.T., and Z. A. Silberston, 1973, *The Economic Impact of the Patent System* (Cambridge, UK: Cambridge University Press).

Tocker, Edwin, 1988, "A Chemical Industry Perspective," Chapter 13 in Charles E. Walker and Mark A. Bloomfield (eds.), *Intellectual Property Rights and Capital Formation in the Next Decade* (Landham, MD: University Press of America), pp. 151-162.

World Health Organization (WHO), International Medical Products Anti-Counterfeiting Taskforce (IMPACT), 2011, *IMPACT Handbook*, IMPACT Secretariat at AIFA (January). Available at: <http://www.who.int/impact/handbook_impact.pdf>, accessed November 3, 2011.

About the Author

Dr. Kristina M. Lybecker is an Assistant Professor of Economics at Colorado College in Colorado Springs. She earned a B.A. from Macalester College, with a double major in Economics and Latin American Studies, and received her Ph.D. in Economics in 2000 from the University of California, Berkeley.

Kristina's research analyzes the difficulties of strengthening intellectual property rights protection in developing countries, specifically the problems related to pharmaceutical counterfeiting and the response of the pharmaceutical industry. Recent publications have also addressed alternatives to the existing patent system, the balance between pharmaceutical patent protection and access to essential medicines, and the markets for jointly produced goods such as blood and blood products.

Kristina has testified in more than a dozen states on the economics of pharmaceutical counterfeiting. She has also worked with US Food and Drug Administration, Reconnaissance International, PhRMA, the National Peace Foundation, the OECD and the World Bank, on issues of innovation, international trade, and corruption.

Appendix 1

Definitions of Each Issue Compared Across Patent Regimes in Table 3.

Taken Directly From: Foreign Affairs and International Trade Canada, "Comparative Chart of Patent Regimes," May 2009.

Basic Patent Term in Years: number of years until patent expiry.
IMPORTANCE: A patentee wants a long patent term to capture the greatest value possible from market exclusivity.

Entitlement to Patent: Legal concept that defines who has the right to receive a patent for an invention.
IMPORTANCE: In a first-to-file system, such as in Canada, the right to the grant of a patent for a given invention lies with the first person to file a patent application for protection of that invention, regardless of the date of actual invention. A first-to-invent system leaves a patent application open to challenges from other inventors claiming they had invented it first.

Patent Term Restoration: A means for a patentee to receive an extra period of patent protection (on top of the regular 20 years) as compensation for regulatory approval delays based on statutory provisions.
IMPORTANCE: Regulatory approval can take years, thus reducing the effective length of patent term. This legislation is designed to promote innovation by allowing innovators to recoup some of the time spent in development of a drug.

Market Exclusivity: Market exclusivity is the period after regulatory approval of a new drug before a generic version can be authorized for sale. Data exclusivity is the period of time during which a generic drug manufacturer is prevented from relying on the innovator's clinical drug trial data that must be submitted to a regulatory agency to prove safety and efficacy of a new drug. Data exclusivity may be the same as or shorter than the market exclusivity.
IMPORTANCE: Data exclusivity is a means for an innovator to obtain market exclusivity for their product by delaying the onset of generic competition.

Early-Working Exception: A provision that allows pre-patent-expiry research or experimental use of the patented medicine (without a patentee's permission) for commercial purposes, including the preparation of a regulatory submission for drug approval.
IMPORTANCE: Reduces the effective market monopoly period for a patentee and enables launch of generic drugs immediately upon patent expiry. On the other hand, this exception allows innovators to conduct experiments using patented competitor products free of patent infringement issues.

Basic Patent Linkage with Automatic Injunction: Regulations that prevent marketing approval (or the pricing and reimbursement status) of generic drugs until after the patents covering the drug product or approved use expire, or until after a court determines that sale of the generic drug would be non-infringing or the patents relating to the brand name drug product expire.
IMPORTANCE: Patent linkage is important for effective patent enforcement, since it provides the equivalent to an automatic injunction against the approval of generics until after patent expiry.

Compulsory Licenses (General): Legislation that allows the government to work or to authorize the working of a patented invention without permission from the patent holder.
IMPORTANCE: Patentees are concerned that patent rights can be easily abused by governments.

Compulsory Licenses (Doha Public Health): The World Trade Organization (WTO) decision, on August 30, 2003, on the Implementation of Paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health and Related Decisions. When implemented in national law, this waiver allows developed countries to authorize the manufacture and export of generic versions of patented pharmaceutical products to countries experiencing public health problems.
IMPORTANCE: Such a provision carries potential for abuse, as the governments themselves decide on the definition of a "public health emergency." The mere existence of a "public health emergency" can be, and has been used, to "arm twist" patent holders into reducing the price of patented drugs or into accepting reduced royalties.

Price Regulation of Patented Drugs: A government body establishes the maximum allowable selling price for patented drugs.
IMPORTANCE: Since the patentee has a monopoly on the particular patented drug, it wants to be able to set the price without government interference.

Interlocutory Injunction in Patent Infringement Court Cases: An interlocutory injunction (also known as a temporary restraining order) is a court order granted at the outset of a court proceeding. It is intended to prevent irreparable damage to a patentee that would be likely to occur if the alleged infringer were allowed to continue the challenged activity during the court trial.
IMPORTANCE: An interlocutory injunction is a powerful tool that provides effective protection for patentees during a court action. Often, the infringing activities of a defendant can be so damaging to a patentee that, by the time the court issues a decision in the infringement trial (which can take years), the plaintiff's business is damaged beyond any hope of recovery. At that point, winning large court awards or bankrupting the defendant would be a pyrrhic victory. To avoid this outcome, an interlocutory injunction orders the defendant, at the onset of the action, to stop the alleged infringing acts during the trial of the action, under the promise of receiving adequate compensation should the court later find in defendant's favour.

Treble Damages for Willful Infringement: A expression that indicates there is a legal basis for a court to triple the amount of the actual/compensatory damages to be awarded to a prevailing plaintiff, generally in order to punish the losing defendant for willful patent infringement.
IMPORTANCE: It is a strong disincentive for would-be patent infringers, especially where the infringer acts willfully (i.e., knowing there was a patent in existence and if infringeding it nevertheless).

Sequence Patents: This refers to the ability to patent gene sequences. Under some more stringent criteria for inventiveness, gene sequences are treated as mere discoveries and not as inventions, thus they are not patentable.
IMPORTANCE: For biotech companies, genetic sequence discovery represents a significant source of intellectual property and shareholder value, thus the ability to patent these sequences can be a significant part of the company's strategy and market value.

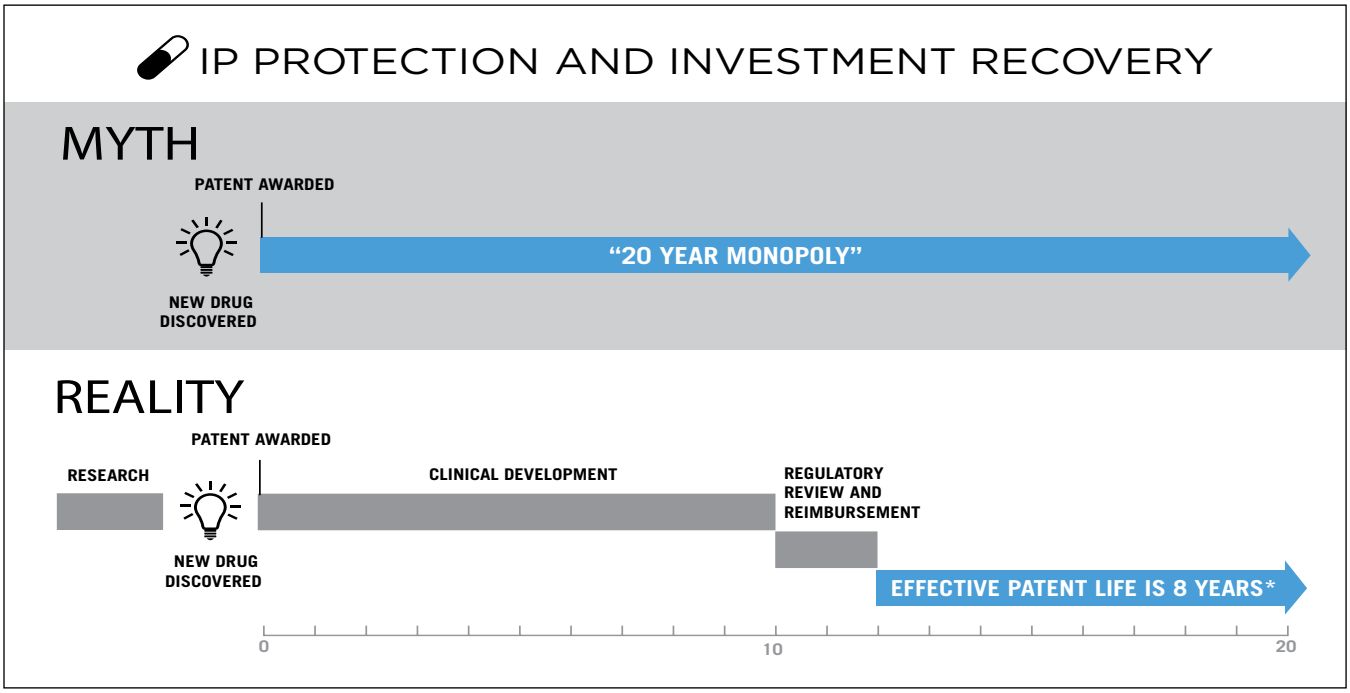
Unusual Subject Matter Restrictions: National patent laws typically place limits on what may be patented. Some restrictions, such as those against patenting abstract principles, theorems, and natural phenomena, help define the term "invention." Others may reflect the country's legal system and or culture and can be controversial and arbitrary, such as diagnostic methods or living transgenic organisms created in a laboratory.
IMPORTANCE: A patentee wants as few restrictions as possible on patentability. Unusual subject matter restrictions can effectively block or narrow down the scope of patent protection in some jurisdictions.

Post-Grant Challenge to a Patent (Administrative): Administrative post-grant challenges to a patent take place in front of an administrative board, and are faster and much less expensive than court litigation.
IMPORTANCE: The existence of an administrative post-grant challenge procedure adds uncertainty for a patentee, casts a cloud on the scope of protection for the patent, and effectively shortens the patent protection. They are favoured by most would-be patent challengers that otherwise lack financial resources for a court trial.

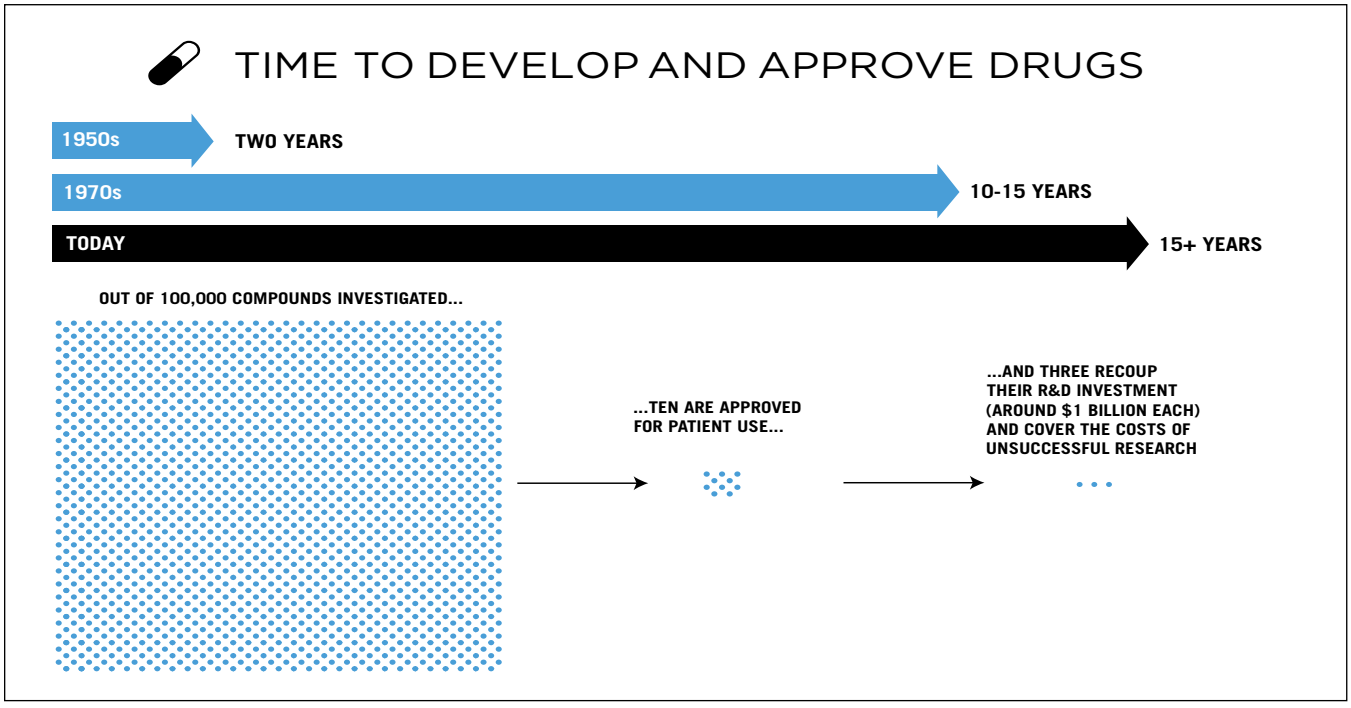
Mandatory Disclosure of Source and Origin for Genetic Resources and Traditional Knowledge:
Statutory requirement that patent applicants must disclose the source and origin of materials and knowledge embedded in an invention, including genetic resources. The stated purpose of these regulations is to prevent "biopiracy" and the monopolization of genetic resources and traditional knowledge through patents, and to provide evidence that the prior informed consent of the local owners of such resources has been obtained and that benefit-sharing agreements have been entered into with those owners.
IMPORTANCE: Mandatory disclosure of source and origin for genetic resources and traditional knowledge represents a major risk to effective patent protection for biotech and pharma products. Inadvertent omission of a small and obscure detail in a patent application could result in either the denial or invalidation of a patent.

Biosimilars/Subsequent Entry Biologics (SEB) Approval Framework: A regulatory process that allows for the development and approval of generic versions of off-patent biologic drug products.
IMPORTANCE: Several high-selling brand-name biologic drugs will come off patent in the next 5 years and patents for other brand-name biologic drugs have already expired. Biotechnology patentees oppose the very concept of biogenerics, as they assert that it would be impossible to replicate the biology leading to the similar product in a generic setting. If a generic version is delayed or not approved by the regulators, a biologic drug could enjoy a degree of exclusivity in the market even after the expiration of its patent. Since the generic competition is the main danger to an innovator drug company's ability to maintain monopoly pricing of its product in the market, it becomes clear that any delay in the introduction of generic competition has a major positive benefit to the bottom line of an innovator.

Patent Protection in Canada: How Long Does it Really Last?



** Average year for market entry (Grootendorst and Di Matteo, "The Effect of Pharmaceutical Patent Term Length on Research and Development and Drug Expenditures in Canada," Healthcare Policy, 2007 February; 2(3): 63-84); the number can vary.*



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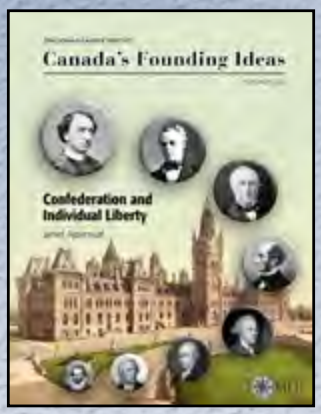

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