The Canada-European Union Comprehensive Economic & Trade Agreement

An Economic Impact Assessment of Proposed Pharmaceutical Intellectual Property Provisions

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Executive Summary

Canada and the European Union (EU) are currently negotiating a comprehensive trade agreement (CETA). As part of these negotiations, the EU has tabled proposals that would significantly alter Canada's intellectual property (IP) regime for pharmaceuticals. This study examines how the proposed EU language in the draft negotiating text would affect the pharmaceutical market in Canada.

Our key finding is that the EU proposals will considerably lengthen the period of exclusivity for innovative drugs in Canada, so that Canada would have the most extensive structural protection of innovative drugs of any country in the world. **Payers – consumers, businesses, unions and government insurers – would face substantially higher drug costs as exclusivity is extended on top-selling prescription drugs, with the annual increase in costs likely to be in the range of $2.8 billion per year.** The annual incremental costs to Canadians in each province are as follows:

PROVINCE	ANNUAL COSTS (MILLIONS OF CANADIAN DOLLARS)
Alberta	211.5
British Columbia	249.1
Manitoba	79.8
New Brunswick	52.2
Newfoundland and Labrador	46.4
Northwest Territories	2.6
Nova Scotia	95.0
Nunavut	1.7
Ontario	1204.4
Prince Edward Island	10.4
Quebec	772.6
Saskatchewan	72.3
Yukon	1.9
TOTAL	**2800.0**

A substantial share of the costs of the EU's proposed changes to IP would fall on government drug plans, which cover approximately 45% of total prescription drug spending in Canada.

This paper lays out the pharmaceutical provisions in the draft negotiating text in the context of Canadian and international standards. It then explores how the provisions, if adopted, would affect public and private sector health-care costs if implemented.

It also conducts case studies of the specific impact on Canadian expenditures for four top-selling prescription drugs that were recently genericized – Norvasc (amlodipine), Lipitor (atorvastatin), Reminyl ER (galantamine ER) and Altace (ramipril) – as well as two drugs that are not yet available in generic versions – Crestor (rosuvastatin) and Plavix (clopidogrel). These case studies demonstrate how the proposed CETA provisions would work in individual cases.

The purpose of exclusivity rights granted to innovators is to create an incentive for research and development investments into new drugs. However, the amount of additional investment in pharmaceutical innovation that would result from the implementation of the EU's proposed pharmaceutical IP provisions would be a small fraction of the additional costs to Canadians. This study finds that $8 of additional drug premiums for Canadians would be needed to generate every $1 of R&D investments by brand-name drug companies. Extending exclusivity periods beyond the current level in Canada, therefore, appears to be an expensive way of encouraging such investments.

1. Introduction

Canada is currently engaged in negotiations with the European Union (EU) to enter into a Comprehensive Economic & Trade Agreement (CETA). CETA covers a broad range of activities, including trade in goods and services, investment, government procurement, regulatory cooperation, temporary entry of business persons, competition policy, labour, and the environment.[1] The draft negotiating text also includes a chapter on intellectual property (IP) with several provisions that specifically relate to the pharmaceutical industry. This paper focuses on the economic benefits and costs of the intellectual property provisions proposed by the EU with respect to the pharmaceutical industry.

Canada and the European Commission conducted a joint study in 2008 on the economic impacts of the agreement's proposed reductions in trade barriers between Canada and the EU, finding substantial annual gains to both economies (European Commission & Canada, 2008). However, that study did not address CETA's pharmaceutical IP provisions. The present analysis addresses this gap.

Pharmaceutical costs are a pressing issue in Canada. Healthcare costs are rising as Canada's population ages, and pharmaceuticals comprise a significant and growing percentage of these costs. A recent report indicates that the drug sector will be the second largest component of Canadian healthcare spending in 2010 – ahead of physicians – at more than $31 billion.[2] (All dollar values in this paper are in Canadian currency.) Sales of patented drugs were approximately $13 billion in 2009. Canadian public drug plans have been at the forefront of efforts to control drug spending, with the creation of the Common Drug Review, with the use of special reimbursement mechanisms such as reference pricing, and with various efforts to control prescribing volume. Most recently, several provinces have set lower regulated or negotiated prices for generic drugs, leading to system-wide generic price reductions of as much as 50 percent (in the case of Ontario and Quebec), yielding annual savings in the hundreds of millions of dollars. Specific consideration of the impact of the agreement's intellectual property provisions on the pharmaceutical market is therefore warranted.

The study examines the impact of the changes on Canada's pharmaceutical market – consumers, payers, and industry. While there will be costs and benefits to various parties, we find that the provisions proposed by the EU will create substantial costs for payers – including the provinces – matched by increased revenues for brand name pharmaceutical manufacturers, which are primarily based outside of Canada.

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[1] "Minister Day Announces Crucial Step Forward on Canada-EU Comprehensive Economic Agreement", Foreign Affairs and International Trade Canada, 5 March 2009,

http://www.international.gc.ca/media_commerce/comm/news-communiques/2009/386908.aspx?lang=eng.

[2] CIHI 2010 "Health care spending to reach $192 billion this year." Last accessed 10 December 2010 at http://www.cihi.ca/CIHI-ext-portal/internet/en/Document/spending+and+health+workforce/spending/RELEASE_28OCT10

If Canada agrees to the proposed EU IP provisions in CETA, Canada would provide the longest structural protection to patented drugs in the world. Canada would become the only country combining a patent linkage regime, automatic patent term extensions, and ten-plus years of data exclusivity.

One reason for the EU's interest in increased protection for innovative pharmaceutical products is that many pharmaceutical companies are headquartered in the EU. Canada's trade with the EU favours European producers: Canada imported $5.3 billion of pharmaceutical products from the EU in 2009, and exported $1.3 billion to the EU.[3] Evidently, patent-protected pharmaceutical exports to Canada should be important to EU CETA negotiators.

Exclusivity is a tool countries can use to encourage and reward investment in innovation. Providing richer rewards through longer exclusivity periods can encourage more innovation. This paper does not comment on the merit or appropriate length of exclusivity period for new drugs but focuses on the likely cost of implementing the EU's pharmaceutical IP policies, and offers commentary on the likely effects on pharmaceutical R&D and manufacturing investments (made globally and domestically).

The Status of the CETA Negotiations

The launch of negotiations toward CETA was announced at the Canada-EU Summit on May 6, 2009. To our knowledge, there have been no formal negotiations regarding the pharmaceutical-related IP provisions since the EU first made proposals in the first round. The leaked text on which this analysis is predicated represents the EU's negotiating position and is not necessarily the basis for a final agreement.[4]

[3] Currency figures are taken from European Commission Trade Website – "Canada (Bilateral relations) Statistics - September 2010, http://trade.ec.europa.eu/doclib/docs/2006/september/tradoc_113363.pdf. Canadian dollar figures are based on the Canadian dollar-Euro exchange rate prevailing at December 31, 2009.

[4] Text available for download at http://tradejustice.ca/en/section/3.

2. Current regulations protecting innovative pharmaceuticals

A primary aspect of pharmaceutical policy for a country is the exclusivity protections offered by its government to innovative drugs. Exclusivity is offered as an inducement to innovation: the firm that develops and brings a new drug to market is rewarded by the grant of a temporary government-sanctioned monopoly. For decades, this process has yielded generations of new drugs that have delivered substantial gains in health. Innovative drugs can deliver incremental or even breakthrough value over existing therapies. At the same time, the financial sustainability of health-care systems is affected by pharmaceutical costs, which constitute a substantial share of total Canadian health care costs.

Pharmaceutical exclusivity periods rely on three key legal regimes in Canada: the *Patent Act*, the *Patented Medicines (Notice of Compliance) Regulations*, and Data Exclusivity, referred to as "Data Protection" in Canada's *Food and Drug Regulations*. The interaction between these different regulations makes this a complex area of law and policy. We therefore describe the current Canadian pharmaceutical IP regime briefly below.

Patents

Pharmaceutical firms can apply for patents to obtain 20 years of exclusivity for an invention disclosed in a patent, as in all other sectors. The invention must be novel, useful, and not obvious to a person "skilled in the art." Typically, commercially successful drugs have many patents filed relating to them, with the filing occurring at different times, leading to different expiry dates. This multiplicity of patents arises because pharmaceuticals can be very complex to develop, embodying many different technologies in their development, the process of manufacturing, and in their attributes.

Patent Linkage

Canada's patent linkage regulations – the *Patented Medicines (Notice of Compliance) Regulations* ("*NOC Regulations*") – create a connection between the regulatory approval of generic drugs and patents. In short, a company wishing to bring a generic drug to the Canadian marketplace must address patents asserted to be relevant by the patent owner (the "brand company"), before Health Canada will issue marketing authorization. For any given patent, a generic company can either await expiry or allege that the patent is invalid or not infringed. If it chooses the latter path, there will be a judicial proceeding in which the merits of the allegations are assessed in the Federal Court.

Canada's unique patent litigation regime (with a patent linkage system often followed-up by full patent infringement actions) mean that generic companies may have to litigate a single brand patent twice – first, they may face litigation to determine patent validity under the *NOC Regulations*; and second, after launching, they risk being sued for infringement under Canada's *Patent Act*. Similarly, a brand company that wins under the *NOC Regulations* may be forced to defend a patent's validity again in a patent impeachment action. As noted by Industry Canada when it amended the *NOC Regulations* in 2006:

> [This] double jeopardy arises because the NOC system is intended to provide a rapid resolution, and so does not allow a comprehensive exploration of the patent's validity. Thus, for some products there are multiple court proceedings, with the resulting additional litigation costs inevitably transferred onto consumers. The *NOC Regulations* are one aspect of the Canadian government's attempt to create a "balance between effective patent enforcement over new and innovative drugs with the timely market entry of their lower-priced generic competitors."[5]

Data Exclusivity

Canadian law protects innovative drugs for a period of eight years from generic competition through the protection of innovator data. The idea is that, during this period, 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. There is also a six-month extension granted for innovative products that have been the subject of clinical testing in pediatric populations.

Data exclusivity in Canada is currently restricted only to certain drugs meeting specific criteria, and does not apply to new uses for existing drugs.

The policy motivation for data exclusivity is that clinical testing is extremely expensive – approximately half the total cost of developing a new drug and bringing it to the point of approval – but such testing is generally not covered by patents. Thus, in the case where patents are for some reason inadequate to protect the product's exclusivity for a reasonable period of time, data exclusivity may still provide a motivation to a firm to invest in the clinical trials required to bring the product to the point of approval.

The combination of these three types of exclusivity protections is specifically tailored to the pharmaceutical industry's unique structure, in which extensive bench science is followed by lengthy and very costly clinical trials, and in which generic firms are able to obtain substantial market share upon being listed on provincial formularies. There have been frequent adjustments to the system in Canada over the course of many years, evidently made to ensure that Canada is an attractive place to invest in R&D, that it fulfills its international obligations under the World Trade Organization's *Agreement on Trade-Related Aspects of Intellectual Property Rights* (TRIPS) and under the *North American Free Trade Agreement* (NAFTA), and that the exclusivity rights are consistent with a financially sustainable health-care system.

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[5] Regulatory Impact Analysis Statement accompanying the 2006 amendments to the *Patented Medicines (Notice of Compliance) Regulations*.

3. The EU's Proposed Pharmaceutical IP Provisions

The intellectual property provisions in CETA currently proposed by the EU would require substantial changes in Canada's IP laws for pharmaceuticals. If Canada agrees to the EU's proposed pharmaceutical provisions in CETA, it will have the highest legislative or structural protection for new pharmaceuticals in the world, as shown in the chart below and explained in more depth in the following subsections. Canada would become the only country to combine a patent linkage regime, automatic patent term extensions, and ten-plus years of data exclusivity.

TABLE 1: COMPARATIVE SUMMARY OF PHARMACEUTICAL INTELLECTUAL PROPERTY PROVISIONS

	TRIPS REQUIREMENT?	USA	EU (NOW)	EU (CETA)	CANADA (NOW)	CANADA (CETA)
Patent Term	20 years	20 years	20 years	20 years	20 years	20 years
Patent Linkage[6]	NO	YES	NO	NO	YES	YES
Finality to Patent Linkage Proceedings[7]	N/A*	YES	N/A	N/A	NO	NO
Patent Term Extension	N/A	0 - 5 years (limited; requires due diligence)	0 - 5 years	0 - 5 years	N/A	0 – 5 years
First-Generic Exclusivity[8]	N/A	180 days	N/A	N/A	NO	NO
Data Exclusivity[9]	Allowed	5	8 + 2 + 1[10]	8 + 2 + 1	6 + 2 + 6 months	8 + 2 + 1

* N/A = not applicable

[6] In both Canada and the US, any challenge to a patent involves an automatic injunction preventing the drug regulating In both Canada and the US, any challenge to a patent involves an automatic injunction preventing the drug regulating authority from approving the generic drug submission. In the US, approval is prevented for a period of 30 months; in Canada, approval is prevented for a period of 24 months. Any additional injunction sought by a brand company on the basis of a patent must be sought in a Federal court in the relevant country. Most countries do not link the approval of a pharmaceutical product to the existence of a patent.

[7] "Finality" indicates whether a finding under a patent linkage proceeding (to determine whether approval may be issued to a generic) is determinative of the patent status. In the US, which has a linkage system, the linkage proceeding is a full-blown patent infringement proceeding that is determinative of patent validity and infringement issues. However, in Canada, as described above, a finding in a NOC proceeding is not determinative, and even if a patent is found to be invalid in such a proceeding, the patent is still valid for every other purpose, and the patentee may still sue for infringement. This situation reduces incentives for generic entry in Canada, since a generic that has been successful in entering is still at risk of paying substantial damages to a patentee for infringement.

In some cases, as outlined below, the EU has made non-reciprocal demands – demands that oblige Canada while placing no similar obligation on the EU. Notably, the EU's proposed language for CETA's IP Chapter will require no changes to the EU's present pharmaceutical regulatory system, and will not require the EU and its member states to adopt all the standards demanded of Canada.

It is useful to compare Canadian generic market authorization dates with those in the US to help assess whether Canada is currently out of step with its most significant trading partner. Comparison with the EU is more challenging due to the fragmentation of generic markets across EU member countries.

In 2010, 15 molecules which had been solely available as branded products received a NOC in Canada. Of those, 13 were products that were also authorized for sale in the US. Out of those 13 products, six were authorized for sale in the US before generic competition was possible in Canada. The products, and their dates for first generic market authorization in Canada and the US, are shown in Table 2. At least for these products, Canada's current framework for protecting pharmaceutical exclusivity appears to be roughly in line with that of the US.

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[8] First-Generic Exclusivity" is a mechanism for incentivizing generic firms to challenge patents. If the first-filing generic is successful in showing that the remaining patents are either invalid or not infringed, it is given approval to market its product and no other generic firms are permitted to enter for 180 days. This creates a strong incentive for generic firms to challenge weak or frivolously listed patents. Only the United States has created such a system.

[9] The nature, scope and extent of the "data exclusivity" regimes across countries differ in various ways. For example, in the United States, companies conducting new and essential clinical trials after a product has been approved can obtain three years of exclusivity limited to the approved change resulting from the trials; however, this does not prevent generic approval for bioequivalent versions of the originally-approved brand product. As well, the United States treats biologics differently from small molecules, providing 12 years of exclusivity for new biologics.

[10] EU member states currently have varying periods of data exclusivity. Directive 2004/27/EC introduced a new data exclusivity extension of 8+2+1, which will not impact generic applications until after October 2013. A six year data exclusivity provision is still effectively applied today in the following EU member states for current generic medicines applications: Austria, Denmark, Finland, Ireland, Portugal, Spain, Greece, Poland, Czech Republic, Hungary, Lithuania, Latvia, Slovenia, Slovakia, Malta, Estonia and Cyprus. Non-EU countries Norway, Liechtenstein and Iceland also provide six years of data exclusivity.

TABLE 2: DATES OF FIRST GENERIC NOC FOR 15 PRODUCTS IN CANADA IN 2010

MOLECULE	BRAND PRODUCT	CANADA FIRST GENERIC APPROVED (NOC)	US FIRST GENERIC APPROVED (NOA)	CANADIAN GENERIC ENTRY LATER
Atomoxetine	Strattera	09/16/10	08/30/10	Yes
Atorvastatin	Lipitor	05/19/10	11/30/11	No
Cilastatin Sodium/ Imipenem	Primaxin	05/20/10	Not yet approved	No
Dorzolamide/Timolol	Cosopt	02/12/10	10/28/08	Yes
Finasteride	Proscar	01/29/10	07/28/06	Yes
Galantamine ER	Reminyl ER	11/12/10	08/28/08	Yes
Letrozole	Femara	04/07/10	12/24/08	Yes
Nabilone	Cesamet	11/01/10	Not yet approved	No
Nevirapine	Viramune	11/16/10	Not yet approved	No
Ramipril HCTZ	Altace HCT	02/02/10	N/A*	
Repaglinide	GlucoNorm	07/26/10	Not yet approved	No
Risedronate	Actonel	01/27/10	10/05/07	Yes
Risedronate+Calcium	Actonel + Calcium	07/28/10	N/A	
Rosiglitazone/ Metformin	Avandamet	12/21/10	Not yet approved	No
Sildenafil	Revatio	06/08/10	Not yet approved	No

*N/A = Not applicable

Notes: The dates for the first US generic approval are abstracted from the Orange Book, with the exception of the US generic approval for atorvastatin. Generic entry for atorvastatin is expected in the US on November 30 2011 pursuant to a settlement of worldwide litigation. Ramipril HCTZ and Risedronate + Calcium are not listed in the Orange Book as brands or generics. The dates for the first Canadian generic approval are based on the date in which Health Canada issued the first generic NOC. From a legal perspective, the issuance of an NOC means the product can be sold in Canada. It should be noted that, at the time of publication, some of these products had yet not been launched in the Canadian market by generic companies. As discussed in section 2 of this report, Canada's pharmaceutical IP regime allows for dual litigation on the same patents – both in an NOC proceeding that determines whether the generic can enter the market and in a patent infringement action that determines the validity of the patent(s) in question. This creates a situation whereby generic companies face a financial risk in launching generic products in Canada. Such a dual litigation scenario is not a feature of the patent linkage system in the United States.

The intellectual property provisions of the European Union's draft CETA IP Chapter that are most relevant to the pharmaceutical market in Canada are:

1. Patent Term Extension (Article 9.2)

2. Data Exclusivity (Article 10)

3. Rights of Appeal under Canada's Patent Linkage Regime (Article 10.4)

4. Border Measures (Article 30)

The section below describes the EU's proposed CETA language and the expected impact on Canada in detail.

Extended Patent Term

Proposed Article 9.2 provides up to five years of automatic additional protection after a patent expires (plus six months if paediatric studies have been carried out) for drug products requiring marketing approval, where the time period a patent-protected product is on the market has been shortened by the lapse of time between the filing of a patent and the granting of market authorisation by Health Canada, even if the innovator is responsible for the delay.

EU Proposed Treaty Text

Article 9.2 – Supplementary Protection Certificates

The Parties recognize that medicinal and plant protection products protected by a patent on their respective territory may be subject to an administrative authorisation procedure before being put on their market. They recognise that the period that elapses between the filing of the application for a patent and the first authorisation to place the product on their respective market, as defined for that purpose by the relevant legislation, may shorten the period of effective protection under the patent.

The Parties shall provide a further period of protection for a medicinal or plant protection product which is protected by a patent and which has been subject to an administrative authorisation procedure, that period being equal to the period referred to in paragraph 1 second sentence above, reduced by a period of five years.

Notwithstanding paragraph 2, the duration of the further period of protection may not exceed five years.

A medicinal product for which paediatric studies have been carried out may be entitled to a six months extension of the period mentioned in paragraphs 2 and 3.

Current State of Canadian Law

Canada currently does not provide patent term extensions for delays in attaining marketing approval for a product. Canadian patents in all fields of technology have 20-year terms from the date the patent is filed, which is the uniform patent term standard set under TRIPS.

Impact of CETA Provision on Canada

The EU's proposed language would result in Canada effectively granting up to 25.5 years of patent life for many pharmaceutical patents on approved products. The language is vague and it is not clear whether it could be made to apply retroactively to patents that have already expired. Patent term extension would appear to be available even in circumstances where a company delays the initial filing of its Canadian product submission.

The EU's proposed patent term extension provision specifies neither which patents covering a pharmaceutical product are eligible for extension, nor how many patents can be extended per product. These issues have been dealt with in the EU and the United States under their patent term extension regimes:

- In the EU, patent term extensions are called "supplementary protection certificates", or SPCs. SPCs are available for a "basic patent" on a product. This has been interpreted flexibly to include not only genus patents for the original discovery of new compounds but also patents covering "best in class" compounds selected from the broader class, such as enantiomers, as well as variants of existing products that involves a therapeutic difference in the active ingredient. The focus is on the ingredient – a new use of an existing active ingredient does not yield a new "product", for patent extension purposes.[11]
- In the United States, brand companies are entitled to one patent term extension per product, and may exercise their discretion regarding the patent on which they will seek an extension. Similar to the EU, patent term extension is available for new products – including enantiomers, esters or other prodrugs – but not combinations of existing products.[12]

In our analysis of the likely effect of patent term extensions in Canada, we have assumed that any patent term extension regime introduced in Canada would be similar in nature to the EU and US systems.

Data Exclusivity

The EU's language proposes multiple changes to Canada's data exclusivity regime. The most significant provision is Article 10.2, which requires Canada to provide at least 10 years of protection against the commercial use of data that was used for the initial approval for the pharmaceutical product. Health Canada would also not be able to receive an application for approval of a generic product until at least eight years after the brand receives initial marketing approval.

There is also provision for a possible additional year of protection if the brand receives approval for a new therapeutic indication in the EU or Canada within the first eight years of the protection. The language applies broadly to all data submitted to Health Canada in relation to any pharmaceutical product.

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[11] *Generics (UK) Ltd v Daiichi Pharmaceutical Co Ltd & Anor* [2008] EWHC 2413 (Pat) (15 October 2008).

[12] *Ortho-McNeil Pharm., Inc. v. Lupin Pharms., Inc.*, 603 F.3d 1377 (Fed. Cir. 2010); *PhotoCure Asa v. Kappos*, 603 F.3d 1372 (Fed. Cir. 2010); *Pfizer, Inc. v. Dr. Reddy's Laboratories, Ltd.*, 359 F.3d 1361 (Fed. Cir. 2004).

EU Proposed Treaty Text

Article 10 – Protection of Data Submitted to Obtain an Authorisation to put a Pharmaceutical Product on the Market

The Parties shall guarantee the confidentiality, non-disclosure and non-reliance of data submitted for the purpose of obtaining an authorisation to put a pharmaceutical product on the market.

For that purpose, the Parties shall ensure in their respective legislation that any information submitted to obtain an authorisation to put a pharmaceutical product on the market will remain undisclosed to third parties and benefit from a period of at least ten years of protection against unfair commercial use starting from the date of grant of marketing approval in either of the Parties.

(a) during a period of at least eight years, no person or entity (public or private), other than the person or entity who submitted such undisclosed data, will, without the explicit consent of the person or entity who submitted this data, rely directly or indirectly on such data in support of an application for the authorisation to put a pharmaceutical product on the market;

(b) during a ten-year period, a marketing authorisation granted for a subsequent application will not permit placing a pharmaceutical product on the market, unless the subsequent applicant submitted his/her own data (or data used with the authorisation of the right holder) meeting the same requirements as the first applicant. Products registered without submission of such data would be removed from the market until the requirements were met.

In addition, the ten-year period referred shall be extended to a maximum of eleven years if, during the first eight years after obtaining the authorisation in either of the Parties, the holder of the basic authorisation obtains an authorisation for one or more new therapeutic indications which are considered of significant clinical benefit in comparison with existing therapies.

Current State of Canadian Law

Until 2006, Canada provided five years of data exclusivity preventing Health Canada from directly relying on brand data to approve generic drug applications.

In 2006, Canada enacted new and more comprehensive data exclusivity regulations which provide brand drugs with eight years of marketing protection against generic market entry (and six years before a generic can submit an application for regulatory approval to Health Canada).[13] An additional six-months exclusivity is available for a drug if a study has been designed and conducted to increase knowledge about use of the drug in pediatric populations. The 2006 data exclusivity regulations also ensure that brands will receive this protection regardless of whether the generic applicant relies directly or indirectly on the brand's data.

The eight years of data exclusivity is provided to all drugs that meet the definition of "innovative drug" – namely, a drug that contains a medicinal ingredient not previously approved in a drug by the Minister of Health that is not a variant of a previously approved medicinal ingredient such as a salt, ester, enantiomer, solvate or polymorph. The regulations were enacted to satisfy Canada's obligations under NAFTA and TRIPS, although neither NAFTA nor TRIPS requires protection exceeding five years.[14]

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[13] *Food and Drug Regulations*, C.R.C, c. 870, section C.08.004.1.

[14] C.08.004.1 of the *Food and Drug Regulations* was enacted in 2006 to implement Article 1711 of NAFTA and Article 39 of TRIPS. The Federal Court of Appeal had ruled in *Bayer Inc. v. Canada (Attorney General)*, 87

Impact of CETA Provision on Canada

The EU's proposed language will provide data exclusivity for all pharmaceutical products, not just "innovative drugs". This means that minor changes to a product could result in 10 years of new protection. The language contrasts to the data exclusivity contemplated for "new chemical entities" in NAFTA and TRIPS. There does not appear to be any limitation on data exclusivity for new products that are highly similar to existing products.

The EU's proposed text would also result in Canada having to increase its data exclusivity term, resulting in an additional two years of exclusivity. Further, the EU's proposed language would allow for an additional year of protection if the brand company receives approval for a new therapeutic indication in the EU or Canada having "significant clinical benefit".

The EU's proposals for data exclusivity go beyond Canada's international trade obligations in TRIPS and NAFTA. The United States provides for five years of data exclusivity for small-molecule drugs, meaning that generic drugs available in the US may not be available by statute in Canada for a further five years if 10-year exclusivity is introduced in Canada.

Right of Appeal

Article 10.4 of the EU's proposed language provides that because Canada's drug approval system involves patent linkage, Canada must ensure that brand and generic companies are treated fairly, specifically in respect of their respective rights of appeal from court decisions.

The EU does not have a patent linkage system, and therefore Article 10.4 will only apply to Canada. The EU is not obligated to institute a patent linkage system in Article 10.4 or elsewhere in the proposed CETA language. The EU is therefore insulated from any effects of this clause.

EU Proposed Treaty Language

Article 10.4: If a Party relies on "patent linkage" mechanisms whereby the granting of marketing authorisations (or notices of compliance or similar concepts) for generic medicines is linked to the existence of patent protection, it shall ensure that the patent holders and the manufacturers of generic medicines are treated in a fair and equitable way, including regarding their respective rights of appeal.

Current State of Canadian Law

Under Canada's *Food and Drug Regulations*, the Minister of Health grants approval for the marketing of brand and generic drugs.[15] To obtain approval for a drug, a pharmaceutical company will file a submission with Health Canada. For brand drugs

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C.P.R. (3d) 293 that Canada's pre-2006 data exclusivity regulations met the requirements of both NAFTA and TRIPS.

[15] *Food and Drug Regulations,* C.R.C, c. 870.

the submission is normally a New Drug Submission ("NDS"); for a generic, it is normally an Abbreviated New Drug Submission ("ANDS").

As set out above, the ability for a generic to obtain regulatory approval of its ANDS is "linked" to the protection of intellectual property. Upon review of the generic's ANDS, if the Minister of Health determines the generic drug to be safe and effective, then Health Canada would issue marketing approval called a Notice of Compliance ("NOC"). However, before the Minister can issue the NOC, Canada's linkage regulations, the *NOC Regulations*, require a generic to first address the brand company's patents.[16]

The addressing of patents by the generic (i.e. by alleging they are invalid, not infringed or not properly listed on Health Canada's Patent Register) permits the brand to commence an application for an order prohibiting the Minister from issuing the NOC to the generic. Upon commencement of a prohibition proceeding by the brand, the Minister of Health is automatically prohibited from issuing a NOC to the generic for up to 24 months; this is frequently referred to as a "24-month stay".

If the generic is successful in demonstrating that the brand's patents either do not apply to the generic's product, or the brand's patents are invalid or not infringed, then the Minister of Health must grant the generic a NOC (if the generic drug has already been determined to be safe and effective by Health Canada).

The federal government intended NOC proceedings to be summary in nature and of short duration for the limited purpose of making (or refusing) an order prohibiting the Minister from issuing a NOC. Canadian courts have ruled that NOC proceedings cannot be taken as a final determination of the validity of a patent, are not substitutes for infringement actions, and are not used to set binding precedents on controversial and uncertain questions in patent law.[17] Patent infringement and validity determinations are reserved for patent actions, the same as in any other area of technology.

In reality, though, these cases are lengthy and complex. The Supreme Court of Canada has, on multiple occasions, held that the automatic stay issued to patentees under the *NOC Regulations* is an "extraordinary" remedy, not available to patentees in any industry outside of the pharmaceutical industry.

Although the subject matter of NOC and patent infringement proceedings is similar, there is a clear divide: NOC proceedings address the issuance of NOCs; patent infringement actions address patent infringement and validity.

Both brand and generic companies can appeal a decision in a prohibition proceeding; the *NOC Regulations* do not prevent any appeal. However, an appeal by a brand name company could be found moot on the facts as Health Canada typically issues an NOC to the generic company soon after a prohibition hearing that ends in favour of the generic

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[16] The *NOC Regulations* created a Patent Register whereby an innovator drug company can have patents listed that are relevant to its various drug submissions. The patents listed on the Patent Register are the patents the generic company must address before it can receive regulatory approval.

[17] *Eli Lilly Canada Inc. v. Novopharm Ltd.*, 2007 FCA 359, at paras. 32 and 40-41.

company.[18] That said, the brand company has the legal opportunity to convince the Court otherwise.[19]

Impact of CETA Provision on Canada

Article 10.4 of the EU's proposed language will overrule the common-law of mootness in the case of NOC appeals brought after the NOC has already issued. This could extend the period during which generics are prohibited from entering the market while a court hears and renders a decision on the appeal, which is likely to take between 6-18 months, depending on the Federal Court of Appeal's case load and how quickly the parties prepare material. This undermines the objective that NOC proceedings conclude quickly.

Alternatively, the government could make it possible for Health Canada to revoke an issued NOC and remove a generic drug from the market if the brand name succeeds in its appeal. This option would increase the uncertainty over the issuance of marketing approval for generic drugs and require legislative changes to the *Food and Drugs Act*.

The EU's proposed language seems in some respects superfluous, in that in Canada, the decision in an NOC proceeding is not determinative of the patent. Thus, even if a NOC is granted to the generic, based on a finding of no infringement or patent invalidity in an NOC proceeding, the patentee may still sue the generic for infringement on the same patent under the provisions of the *Patent Act*. Suing for infringement is, in effect, an existing appeal mechanism. In this respect, Canada is unique – as far as we know, there is no precedent for any country in the world to systematically have multiple litigations on the same patents between the same parties.

The EU's proposed language would mean that in Canada, to market a product, generic companies will continue to face the risk of two sets of proceedings, but with full rights of appeal at both stages, in the following sequence:

<u>Pre-generic launch linked to issuance of a NOC</u>

1. Federal Court hearing of an application under the *NOC Regulations*
2. Appeal to Federal Court of Appeal of application
3. (possibly) Appeal to Supreme Court of Canada

<u>Post-generic launch (if appeal by patentee is unsuccessful)</u>

4. Patent infringement / impeachment action under the *Patent Act*
5. Appeal to Federal Court of Appeal
6. Appeal to Supreme Court of Canada

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[18] *Pfizer Canada Inc. v. Apotex Inc. et al.* (2001), 11 C.P.R. (4th) 245 (F.C.A.) at para. 21; application for leave to appeal dismissed with costs [2001] S.C.C.A. No. 111 (S.C.C.); *Merck Frosst Canada Inc. v. Apotex et al.,* [1999] F.C.J. No. 55 (F.C.A.) at paras. 4-6; application for leave to appeal dismissed [1999] S.C.C.A. No. 313 (S.C.C.).

[19] *Abbott Laboratories v. Canada (Minister of Health)*, 2007 FCA 153 (F.C.A.).

Thus, the EU proposal on the right of appeal could result in further litigation costs for both generic and brand companies, as well as additional costs to the court system (in addition to healthcare payer cost increases from generic entry delays, detailed in Sections 4 and 5).

Currently, the NOC regulations allow for damages to be paid to a generic firm that has been kept off the market by a NOC proceeding in which the generic is ultimately successful. The generic may seek lost profits until the date of the NOC judgment, and is thus (at least partially) compensated. The damages provision, however, does not provide for any compensation to be paid to payers who were harmed by paying the brand price instead of the generic price. If the patentee's appeal of an NOC decision had the effect of further delaying generic entry, and if the generic were ultimately successful in its application, consumers and payers (governments and other payers) would not be compensated for any damages caused by the assertion of a patent that was ultimately found to be invalid. In the US, by contrast, consumers, insurance providers and states routinely file suit against brand companies for losses resulting from undue delays in generic entry.[20]

Border Measures

The EU's language would require Canada to adopt a procedure that would allow customs officials to detain shipments of imported drugs at the border where a brand company believes that the product may infringe one of its patents. Customs officials could also detain shipments without a request by the brand company if the customs official has sufficient grounds to suspect violation of an intellectual property right.

EU Proposed Treaty Text

Article 30 – Border Measures

The Parties shall, unless otherwise provided for in this section, adopt procedures to enable a right holder, who has valid grounds for suspecting that the importation, exportation, re-exportation, entry or exit of the customs territory, placement under a suspensive procedure or placement under a free zone or a free warehouse of goods infringing an intellectual property right may take place, to lodge an application in writing with competent authorities, administrative or judicial, for the suspension by the customs authorities of the release into free circulation or the detention of such goods.

The Parties shall provide that when the customs authorities, in the course of their actions and before an application has been lodged by a right holder or granted, have sufficient grounds for suspecting that goods infringe an intellectual property right, they may suspend the release of the goods or detain them in order to enable the right holder to submit an application for action in accordance with the previous paragraph. …

Current State of Canadian Law

Pharmaceuticals are the most highly regulated products in Canada, and the provisions of the *Food and Drugs Act* that ensure safety and efficacy of our drug supply apply to

[20] See for example *In re Wellbutrin SR Direct Purchaser Antitrust Litigation*, US District Court (ED Pen 2004) (No. 04-5525); *American Sales Company, Inc., et al. v. SmithKline Beecham Corporation d/b/a GlaxoSmithKline PLC*, No. 08-CV-03149, E.D. Pa.; *In re Zyprexa Products Liability Litigation*, 493 F. Supp. 2d 571 - Dist. Court, ED.

imported products, including finished dosage forms and active pharmaceutical ingredients.

Health Canada's Health Products & Food Branch Inspectorate, in cooperation with the Canadian Border Services Agency, has the power to detain any products deemed to be illegitimate or counterfeit under the *Food and Drugs Act* and its associated regulations as part of Health Canada's mandate to protect the health and safety of Canadians. This includes pharmaceuticals.

Canada has no law that would grant customs officials with the power to detain shipments at the border on the suspicion that the product may infringe a patent. Patent disputes for pharmaceuticals and all other products in Canada are private legal matters between the purported rights holder and the alleged infringer, and domestic legal recourse is available.

Canada's *Patent Act* and its regulations, which set out the rights of patentees and the public, specifically address how patents may be used in developing and marketing pharmaceuticals. A fundamental feature of Canada's pharmaceutical patent regime permits a generic manufacturer to work patents related to a molecule before the patent expires (by importing, for example) without an NOC. This permission is based on a *quid pro quo*: the patentee can delay issuance of a generic NOC under the NOC Regulations, but the generic manufacturer is permitted to "early work" the patent (by, for example, importing) to do the regulatory work needed to get an NOC once the patent expires or is held invalid or not infringed.

Border measures make more sense for copyright and trade-mark concerns than for patent concerns. From a policy perspective, it would be much harder for a border official to assess possible patent infringement than to assess possible trademark or copyright infringement. This is especially so for pharmaceuticals. Typically, a copyright or trademark counterfeiter wants his product to be mistaken for the true product, and a border official can make a reliable first determination of possible infringement. In contrast, a border official is not equipped to perform a chemical analysis at the border to determine the compounds in a pharmaceutical product, and the border official is not qualified to interpret highly technical patent claims to determine what a patent protects or the validity of those claims. For this reason, implementation of border measures for patents is fraught with difficulty.

This topic was addressed as part of the Anti-Counterfeiting Trade Agreement ("ACTA") negotiations, to which Canada and EU are both parties.[21] The EU was in the minority in attempting to extend border measures to cover patents, and a multilateral consensus has now been reached on this issue. The treaty text was finalized in November 2010 and specifically excluded patents from any such border measures, and it is suggested that Canada and the EU not go beyond the ACTA consensus in CETA.

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[21] "Anti-Counterfeiting Trade Agreement (ACTA)" Foreign Affairs and International Trade Canada, 9 December 2010, http://www.international.gc.ca/trade-agreements-accords-commerciaux/fo/intellect_property.aspx

Impact of CETA Provision on Canada

Border officials would have the power, and in fact be required, to detain shipments of pharmaceutical products in transit through Canada merely on the suspicion of patent infringement. Similar laws have caused considerable difficulty in the EU, where border officials have detained shipments of pharmaceuticals as they passed through EU ports from India to Latin America. Recent reports have indicated that the EU has agreed to implement measures to prevent this outcome in the future.

The power granted border officials would be akin to those granted to judges when making preliminary injunctions. Judges do not grant preliminary injunctions often. When they do, such decisions are made with an evidentiary record and with legal submissions by both affected parties. The EU's proposed language could result in pharmaceuticals being unlawfully detained at the border, significantly impacting the supply of pharmaceutical products for Canadians and Canadian pharmaceutical companies, wholesalers and pharmacies.

To reasonably implement patent-related border measures in Canada, a new administrative apparatus would have to be designed and implemented, including a body with the ability to quickly make patent-related determinations (or some mechanism to ensure fast access to the Federal Courts). This would be a considerable expense and complication for Canadians and Canadian companies, specifically Canadian pharmaceutical companies which already must contend with multiple rounds of patent litigation.

4. Impact on payers

As the above discussion shows, CETA is a complicated treaty, including with respect to its exclusivity provisions for pharmaceuticals. However, what is clear is that the pharmaceutical provisions will have the effect of lengthening exclusivity periods for some drugs, in some cases for many years. This will increase costs for those drugs, with potentially large financial impacts on consumers and insurers – particularly on the provinces, which run the largest drug benefit programs in the country. These financial costs to payers will largely be matched by financial benefits to patentees.

As a preliminary comment, payment for pharmaceuticals is complex in Canada because of varying insurance programs. CIHI (2010, p. 10) estimates that in 2009, public insurers contributed $11.4 billion (or 45%) for prescribed drugs; private insurers contributed $9.4 billion (37%); and households contributed $4.6 billion (18%). We expect that the impact of extended exclusivity would be shared across the three groups in about the same proportions. Ultimately this distinction between payers is somewhat contrived: the same individual will fund provincial insurance through taxes; will fund a private insurance plan through an employment contract; and will pay out-of-pocket for co-payments.

A straightforward approach to assess the cost of the EU's proposed exclusivity extensions is to examine how these extensions would affect the overall patented drug market in Canada. As further described below, the total cost to Canadians of the EU's proposed provisions can be estimated at approximately $2.8 billion per year. Facing these increased costs, it seems likely to us that payers will respond by introducing additional cost controls, such as by increasing patient charges or by restricting access to new prescription drugs.

To determine the average increase in the length of market exclusivity resulting from CETA, 15 drugs for which the first generic NOC was granted in 2010 were considered. The patent, exclusivity and litigation details of these products are described in Appendix III. The likely date of generic entry for each product had the entire set of CETA provisions been in force was estimated. On average, for these products, it is estimated that these provisions would have delayed generic entry by 3.46 years.[22] Table 3 summarizes the impact on projected entry timing for these 15 drugs.

[22] We have attempted to be conservative here; a reasonable alternative assumption on the litigation for one product, dorzolamide, would have increased the average to 3.9 years.

TABLE 3: DELAY IN GENERIC NOC DATE THAT WOULD HAVE RESULTED IF CETA PROPOSALS WERE IN EFFECT IN 2010

MOLECULE	BRAND PRODUCT	ACTUAL GENERIC NOC	LIKELY GENERIC NOC WITH PROPOSED CETA PROVISIONS	DIFFERENCE IN DAYS
Atomoxetine	Strattera	09/16/10	12/24/14	1560
Atorvastatin	Lipitor	05/19/10	08/20/12	824
Cilastatin Sodium/Imipenem	Primaxin	05/20/10	08/08/15	1906
Dorzolamide/Timolol	Cosopt	02/12/10	02/12/10	0
Finasteride	Proscar	01/29/10	11/11/12	1017
Galantamine ER	Reminyl ER	11/12/10	11/08/15	1822
Letrozole	Femara	04/07/10	04/27/15	1846
Nabilone	Cesamet	11/01/10	11/01/10	0
Nevirapine	Viramune	11/16/10	11/16/10	0
Ramipril HCTZ	Altace HCT	02/02/10	07/13/16	2353
Repaglinide	GlucoNorm	07/26/10	07/15/11	354
Risedronate	Actonel	01/27/10	01/27/16	2191
Risedronate+Calcium	Actonel + Calcium	07/28/10	05/17/16	2120
Rosiglitazone/Metformin	Avandamet	12/21/10	02/13/13	785
Sildenafil	Revatio	06/08/10	05/26/16	2179
			Average in days	1264
			Average in years	3.46

Estimating the counterfactual date of generic entry is a complex exercise, since each product has different patents and a different history of litigation. Attempts were made to obtain a reasonable measure of the likely date of generic entry had CETA been in force. This analysis is not immune to attack: many judgments were made regarding how CETA would have applied, and it could be argued that CETA would likely have led to earlier or later entry than estimated for each product. However, it is our view that the average is reasonably robust. The assumptions underlying this analysis are detailed in Appendix III.[23]

Total Canadian expenditure on patented drugs is approximately $13.3 billion annually (PMPRB 2010). The average pharmaceutical product benefits from exclusivity for approximately 10 years; thus extending exclusivity by one year would have the effect of increasing revenues of patentees by one tenth.[24] Using these two rather approximate

[23] The analysis in Appendices I, III, and V was performed at our request by Gilbert's LLP.

[24] The average time from first brand NOC to first generic NOC for the 15 products genericized in 2010, as shown in Appendix III, is 9 years. Typically, new chemical entities obtain longer approval periods than other approved drugs. The recently released report by the Canadian Intellectual Property Council titled "Innovation for a Better Tomorrow" assumes that average exclusivity periods are from 7-9 years. If we were to assume that the average period of exclusivity is eight years, then extending exclusivity by one year implies that we would increase the revenues to the patentee by one eighth, or approximately $1.6 billion. We have chosen a conservative assumption that one additional year of exclusivity will increase patentee

figures, it can be inferred that the effect of extending exclusivity by one year on the revenues of patentees in Canada would be approximately $1.33 billion annually, given no change in prices or insurance coverage decisions. Assuming the average price after the end of exclusivity to be 39% of the brand price[25], the increased cost to payers of each additional year of exclusivity is approximately $811 million dollars annually.

Thus, if the average exclusivity period is extended by 3.46 years (as estimated above), the increase in annual cost to payers would be approximately $2.8 billion per year, calculated as follows:

Total Annual Brand Sales	$13.3 billion
x % Sales Going Generic	x 0.1
Annual Brand Sales Losing Exclusivity	$1.33 billion
x 61% Price Discount	x 0.61
Annual Loss from 1 Year Entry Delay	$811 million
x Number of Years Delay	x 3.46
Total Annual CETA Delay	**$2.8 billion**

This calculation can of course be adjusted. If there were fewer new drugs with exclusivity in the future, the financial impact of extensions would be smaller. If the average price after the end of exclusivity were relatively higher or lower, that would reduce or increase the impact on payers. The estimate also depends on the average extension to exclusivity periods: the longer the extension, the greater the additional cost.

We provide in Table 4 an approximate decomposition showing how these costs would be allocated between the public and private sectors in the different provinces. The public sector includes both provincial and federal government expenditures; while the private sector includes private insurance and out-of-pocket payments by patients. We have assumed, for the purpose of this analysis, that the average price following generic entry falls by 61%.[26] The allocation of costs across provinces is based on CIHI's analysis of expenditures on prescription drugs in Canada, and the methodology is described in Appendix II.

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revenues by one-tenth. This "one-tenth" estimate is additionally conservative as it can be expected that products' annual revenue will be highest toward the end of their exclusivity periods, after physicians have become comfortable prescribing the drug and more information about its effects are known.

[25] See Appendix IV for detailed pricing assumptions. 61% is the average assumed discount, calculated as the average price discount achieved by different payers, weighted by their share of total prescription drug purchases.

[26] We have assumed that the average price in Ontario and Quebec falls by 65%; the average price in British Columbia, Saskatchewan and Manitoba, by 55%; and the average price in all other jurisdictions by 50%. While on average generic price reductions are expected to be larger than this, these rates also allow for some branded product to continue to be sold at the original high price. We have also assumed that both private and public sectors obtain the same average price in each province; with public reimbursement typically being limited to the lowest generic price, it seems likely that the estimates in Table 4 are slightly understating the cost to the public sector, and overstating the cost to the private sector.

TABLE 4: THE ALLOCATION OF THE BURDEN OF PAYING FOR EXTENDED EXCLUSIVITY: ADDITIONAL EXPENDITURES BY PROVINCE AND PAYER TYPE RESULTING FROM EU'S IP PROPOSALS

PROVINCE	PUBLIC ($M)	PRIVATE ($M)	TOTAL ($M)
Alberta	96.1	118.7	214.8
British Columbia	101.2	151.9	253.0
Manitoba	38.0	43.1	81.1
New Brunswick	18.4	34.7	53.1
Newfoundland and Labrador	13.2	20.5	33.6
Northwest Territories	1.3	0.9	2.2
Nova Scotia	30.0	38.9	68.9
Nunavut	0.9	0.6	1.4
Ontario	551.2	671.9	1223.1
Prince Edward Island	3.4	5.3	8.8
Quebec	412.2	372.5	784.6
Saskatchewan	40.3	33.2	73.5
Yukon	1.1	0.8	1.9
Total	**1300.9**	**1499.1**	**2800.0**

Payer responses

There may also be other types of responses to extended exclusivity periods. For example, insurers squeezed by financial constraints due to longer exclusivity might reduce the number of drugs covered – so that while each drug would have longer exclusivity, fewer drugs would be covered by insurance plans. This would be an unambiguously negative outcome, since the overall revenues of patentees would not rise, and fewer drugs would be available to patients. Thus there would be no additional incentive for new drug innovation, and access for Canadian patients would be reduced in this scenario.

Another possible response is that insurers might bargain over price more aggressively, so that longer exclusivity would be balanced by lower prices. If the result were no increase in total spending, the impact on payers and on the incentives for new drug innovation would be zero. Grootendorst and di Matteo (2007) show that provinces did not have very large increases in drug expenditures after the implementation of increased exclusivity periods created by revisions to Canada's patent laws in the 1980s and 1990s. The cost-control measures used included cost-effectiveness analyses, price controls, reference pricing, mandatory generic substitution, and the use of patient co-payments by insurers. Arguably, these measures were responses to the changes in patent law. However, it is not clear whether there is further scope for these kinds of responses.

One perspective on this is that Canada's Research-Based Pharmaceutical Companies (Rx&D), the brand name pharmaceutical industry's trade association, supports longer exclusivity periods. One might infer from this that its members expect that the profits from longer exclusivity periods would not be entirely compensated by reductions in the number of drugs covered or in prices paid.

5. Case studies: six drugs

It is helpful to supplement the general perspective provided above with case studies illustrating how the effects of the EU's proposed pharmaceutical provisions would differ between products and how the costs would vary across provinces. In this section, the impact on how the CETA provisions would have applied to several existing drugs is examined. The protection afforded by the CETA provisions for each product differs, depending on the particular patent and approval situation of each product. So these cases are illustrative. Details of the effect of the EU's proposals on the expected generic market entry dates for each product are provided in Appendix I. Using specific examples is useful since historical data on drug plan specific total unit volumes and prices, as well as specific actual or likely entry dates of competitive supply with and without the EU's proposed language, can be incorporated.

Four of the molecules (Norvasc (amlodipine), Lipitor (atorvastatin), Altace (ramipril), and Reminyl ER (galantamine ER)) have already been genericized. These examples are useful, since they provide a complete picture of how the drugs became available in generic form and illustrate the likely effect of CETA on other drugs in the future. Moreover, three of the four drugs would not have been genericized if CETA had been implemented, these molecules could still be affected by CETA. The remaining two molecules, Plavix (clopidogrel) and Crestor (rosuvastatin), do not yet face generic competition in Canada. For these products, the estimated increases in cost are forecasts of what is likely to happen if CETA's negotiating text is adopted. CETA's text would affect these molecules as follows:

PRODUCT	DELAY FROM CETA IP PROVISIONS
ALREADY GENERIC	
Lipitor (atorvastatin)	2 years extra market exclusivity as the result of a patent term extension and pediatric exclusivity extension
Norvasc (amlodipine)	2 years 4 months extra market exclusivity as the result of a patent term extension and pediatric exclusivity extension
Altace (ramipril)	At least 5 months, and likely longer, of extra market exclusivity as the result of a patent term extension and the ability of brand companies to appeal an NOC proceeding invalidating a compound patent
Reminyl ER (galantamine ER)	At least 4 years 5 months of extra market exclusivity as the result of extended data exclusivity and the ability of brand companies to appeal an NOC proceeding invalidating a dosage regimen patent
NOT YET GENERIC	
Crestor (rosuvastatin)	Predicted 5 years 5 months of extra market exclusivity as the result of a patent term extension, pediatric exclusivity extension, enhanced data exclusivity
Plavix (clopidogrel)	Predicted 5 years 5 months of extra market exclusivity as the result of a patent term extension and pediatric exclusivity extension

As discussed above, the EU has proposed three different forms of extensions to exclusivity – patent term extension, extended data exclusivity, and "right to appeal". It is unclear at this point, which, if any, of these three specific provisions will be implemented. The likely effects on drug plan spending of each of these provisions were, therefore, considered separately. The effects should all of these provisions be implemented was also considered.

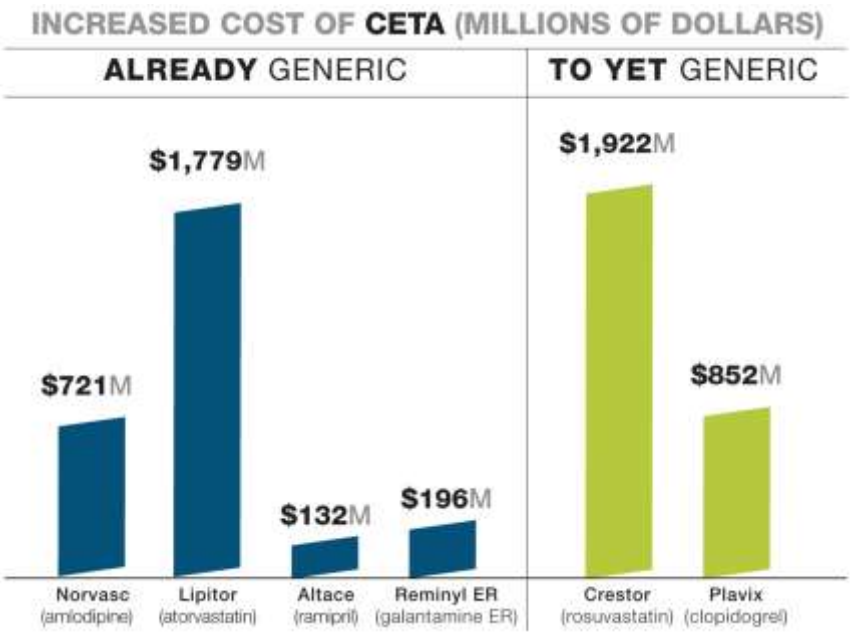
A summary of the effect of each of the EU's proposed pharmaceutical IP provisions on the exclusivity period of the six example molecules is as follows:

TABLE 5: EXAMPLES OF THE EFFECT OF THE EU'S PROPOSALS ON EXCLUSIVITY DATES

ACTUAL OR LIKELY GENERIC ENTRY

PRODUCT	WITHOUT CETA	CETA PATENT TERM EXTENSION	CETA DATA EXCLUSIVITY	CETA NOC APPEAL PROVISION	WITH ALL CETA PROVISIONS
Lipitor (atorvastatin)	May 19, 2010	Aug. 20, 2012	May 19, 2010	May 19, 2010	Aug. 20, 2012
Norvasc (amlodipine)	July 9, 2009	Nov. 9, 2011	July 9, 2009	July 9, 2009	Nov. 9, 2011
Altace (ramipril)	Dec. 13, 2006	May 14, 2007	Dec. 13, 2006	June 27, 2007	June 27, 2007
Crestor (rosuvastatin)	July 2, 2012	Jan. 2, 2018	Feb. 16, 2014	Sep. 16, 2013	Jan. 2, 2018
Plavix (clopidogrel)	Aug. 22, 2012	Aug. 22, 2017	Aug. 22, 2012	Aug. 22, 2012	Aug. 22, 2017
Reminyl ER (galantamine ER)	Nov. 12, 2010	Nov. 12, 2010	Apr. 8, 2015	Nov. 8, 2015	Apr. 8, 2015

Based on the delay periods calculated above, the impact of the proposed pharmaceutical IP provisions of the EU's proposals on expenditures by both public and private drug plans in Canada was forecasted for the drugs listed above. The financial impact of the proposed IP provisions, broken down by province, is set out in detail in the Results section below. The impact on drug costs for the six molecules of interest is represented in the following graph:



Methodology

Data was obtained from IMS Brogan on the unit volumes and drug plan spending (excluding pharmacy dispensing fees but including wholesale and retail markups) of all oral solid dosage forms of these molecules for private and public drug plans, province, and quarter over the period 2001 quarter 1 to 2010 quarter 3. Data were available for shorter time periods for several public plans, including Manitoba (data available to 2010q1), as well as BC, Alberta, Saskatchewan, New Brunswick, Newfoundland and the federal Non-Insured Health Benefit (NIHB) program (data available to 2010q2). The IMS Brogan data are intended to be representative of both public and private plans in each of the provinces.

Simulations were constructed of the additional spending on each of these six molecules if the EU's proposed CETA language had applied (or does apply), for Health Canada's Non-Insured Health Benefits (NIHB), and for private and provincial drug plan spending in each province. (The one exception is the PEI, for which only private plan data were available.) Furthermore, the implications of each of the three proposed forms of IP protection, namely, patent term extension (PTE), extended data exclusivity (EDE), and the right to appeal (RTA) were considered, as were the effects should all of these provisions be implemented (ALL). Appendix I provides information on the actual or likely generic entry dates under the proposed IP provisions of CETA.

Total use is expressed as the number of defined daily doses (DDDs) of the molecule reimbursed by drug plans in Canada. This is the number of milligrams of the drug reimbursed divided by the typical daily maintenance dose of the drug; typical maintenance doses are provided by the World Health Organization Collaborating Centre for Drug Statistics Methodology (http://www.whocc.no/).

Additional drug spending was forecasted as follows. First the total unit volume of each molecule recently observed in each of the plans was extrapolated into future quarters. Specifically, future quarters were assigned the average number of DDDs reimbursed in the most recent 4 quarters of data. (Recall that there are 20 plans and 6 drugs so there were 120 forecasts generated.) DDD volumes were assumed to be unaffected by generic entry.[27] Second, the average price paid per DDD of the drug under five scenarios was predicted: the likely date of generic market entry that would occur in the absence of the EU proposals (hereafter referred to as the "baseline" scenario) and in each of the four scenarios described earlier (PTE, EDE, RTA and ALL). The average price in each scenario was generated by multiplying the price that was assumed to prevail in the absence of generic entry by d, where d is the average reimbursed price divided by the brand price (before generic entry). In quarters preceding generic entry, d is 100%. The range of values of d in public plans was based on current or anticipated provincial policies and the extent to which generic substitution is expected to occur. The value of d is assumed to fall over several quarters because many private plans continue to fully reimburse branded drugs even when the generic product is available. The exact values used are shown in Appendix IV.

The price per daily dose paid in the absence of generic entry was assumed to be the price that prevailed in the quarter immediately prior to observed generic entry. If no generic entry was observed in the data (such as for Crestor (rosuvastatin)), the most recent observation on price available in the data was used.

Having forecasted the total unit volume and reimbursement price of each drug in each of the 5 scenarios for each of the 20 drug plans, it was then possible to forecast additional spending should the proposed EU language in CETA be enacted. For each combination of drug, drug plan and scenario, the present discounted value of spending (discounted at an annual rate of 2% to 2010q3) was assessed. The additional spending under each of the four CETA scenarios (PTE, EDE, RTA and ALL) was then compared to the baseline scenario in which the pharmaceutical IP provisions of the CETA are not enacted.

No adjustment was made for partial quarters.

Results

The following tables show estimates of the additional cost to payers of the proposed IP changes, by province, for each of the molecules. The exclusivity provisions are separated into patent term extension (PTE), extended data exclusivity (EDE), and right to appeal (RTA). The column ALL shows the additional cost to payers if all three proposed policies are implemented.

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[27] We recognize that the number of daily doses for a molecule can be affected by genericization of the molecule. On one hand, lower prices can lead to increased uptake of a drug, due to decreased pricing pressure or the use of drug plan incentives. On the other hand, sales force efforts for products still on-patent in the same drug class can cause physicians to switch from the recently-genericized product to the patented product. This has been the case since genericization of Lipitor (atorvastatin), with patients being switched to Crestor (rosuvastatin) instead. These effects have not been incorporated in the analysis.

In brief, the aggregated extra cost associated with extended exclusivities on the six selected molecules is calculated to be approximately $5.6 billion.

TABLE 6.1 COSTS OF EU PROPOSALS IN CETA FOR ALBERTA, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	60.4	0	0	**60.4**
Lipitor (atorvastatin)	137.2	0	0	**137.2**
Plavix (clopidogrel)	60.9	0	0	**60.9**
Reminyl ER (galantamine ER)	0	10.6	11.7	**11.7**
Altace (ramipril)	11	0	11	**11**
Crestor (rosuvastatin)	145.3	41.2	27.6	**145.3**

TABLE 6.2 COSTS OF EU PROPOSALS IN CETA FOR BRITISH COLUMBIA, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	37.4	0	0	**37.4**
Lipitor (atorvastatin)	142.2	0	0	**142.2**
Plavix (clopidogrel)	80.2	0	0	**80.2**
Reminyl ER (galantamine ER)	0	11.7	12.9	**12.9**
Altace (ramipril)	19.1	0	19.1	**19.1**
Crestor (rosuvastatin)	152.3	43.2	28.9	**152.3**

TABLE 6.3 **COSTS OF EU PROPOSALS IN CETA FOR MANITOBA, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS**

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	23.1	0	0	**23.1**
Lipitor (atorvastatin)	59.1	0	0	**59.1**
Plavix (clopidogrel)	44.7	0	0	**44.7**
Reminyl ER (galantamine ER)	0	1.7	1.9	**1.9**
Altace (ramipril)	3.8	0	3.8	**3.8**
Crestor (rosuvastatin)	53.1	15.1	10.1	**53.1**

TABLE 6.4 **COSTS OF EU PROPOSALS IN CETA FOR NIHB, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS**

NIHB	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	6.2	0	0	**6.2**
Lipitor (atorvastatin)	17.4	0	0	**17.4**
Plavix (clopidogrel)	8.1	0	0	**8.1**
Reminyl ER (galantamine ER)	0	0.1	0.1	**0.1**
Altace (ramipril)	2	0	2	**2**
Crestor (rosuvastatin)	12.4	3.5	2.4	**12.4**

The Non-Insured Health Benefits (NIHB) Program provides, to registered Indians and recognized Inuit, a limited range of medically necessary health-related goods and services which supplement benefits provided through private insurance plans, provincial/territorial health and social programs.

TABLE 6.5 COSTS OF EU PROPOSALS IN CETA FOR NEW BRUNSWICK, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	8.4	0	0	**8.4**
Lipitor (atorvastatin)	27.1	0	0	**27.1**
Plavix (clopidogrel)	16	0	0	**16**
Reminyl ER (galantamine ER)	0	3.6	4	**4**
Altace (ramipril)	3.5	0	3.5	**3.5**
Crestor (rosuvastatin)	42.9	12.2	8.2	**42.9**

TABLE 6.6 COSTS OF EU PROPOSALS IN CETA FOR NEWFOUNDLAND AND LABRADOR, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	3.1	0	**0**	**3.1**
Lipitor (atorvastatin)	18.9	0	**0**	**18.9**
Plavix (clopidogrel)	11.5	0	**0**	**11.5**
Reminyl ER (galantamine ER)	0	**1.3**	**1.5**	**1.5**
Altace (ramipril)	1.5	0	**1.5**	**1.5**
Crestor (rosuvastatin)	44.5	12.6	**8.5**	**44.5**

TABLE 6.7 COSTS OF EU PROPOSALS IN CETA FOR NOVA SCOTIA, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	13.3	0	0	**13.3**
Lipitor (atorvastatin)	29.4	0	0	**29.4**
Plavix (clopidogrel)	17.5	0	0	**17.5**
Reminyl ER (galantamine ER)	0	4.3	4.7	**4.7**
Altace (ramipril)	3.2	0	3.2	**3.2**
Crestor (rosuvastatin)	55.7	15.8	10.6	**55.7**

TABLE 6.8 COSTS OF EU PROPOSALS IN CETA FOR ONTARIO, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	332.3	0	0	**332.3**
Lipitor (atorvastatin)	719.5	0	0	**719.5**
Plavix (clopidogrel)	351.7	0	0	**351.7**
Reminyl ER (galantamine ER)	**0**	113.5	125.5	**125.5**
Altace (ramipril)	60.1	0	60.1	**60.1**
Crestor (rosuvastatin)	827.8	234.8	157.3	**827.8**

TABLE 6.9 COSTS OF EU PROPOSALS IN CETA FOR PEI, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	1.1	0	0	**1.1**
Lipitor (atorvastatin)	2.2	0	0	**2.2**
Plavix (clopidogrel)	1.9	0	0	**1.9**
Reminyl ER (galantamine ER)	**0**	0.3	0.3	**0.3**
Altace (ramipril)	0.3	0	0.3	**0.3**
Crestor (rosuvastatin)	4.1	1.2	0.8	**4.1**

"Note: IMS-Brogan excludes data on the public plan for PEI."

TABLE 6.10 COSTS OF EU PROPOSALS IN CETA FOR QUEBEC, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	216.8	0	0	**216.8**
Lipitor (atorvastatin)	584.2	0	0	**584.2**
Plavix (clopidogrel)	235.3	0	0	**235.3**
Reminyl ER (galantamine ER)	**0**	28.4	31.4	**31.4**
Altace (ramipril)	23.4	0	23.4	**23.4**
Crestor (rosuvastatin)	524.3	148.8	99.7	**524.3**

TABLE 6.11 COSTS OF EU PROPOSALS IN CETA FOR SASKATCHEWAN, SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	18.7	0	0	**18.7**
Lipitor (atorvastatin)	41.3	0	0	**41.3**
Plavix (clopidogrel)	23.9	0	0	**23.9**
Reminyl ER (galantamine ER)	0	1.8	2	**2**
Altace (ramipril)	3.8	0	3.8	**3.8**
Crestor (rosuvastatin)	59.8	17	11.4	**59.8**

Tables 7 and 8 show the impact of the EU's proposed pharmaceutical exclusivity language, aggregating across provinces and drugs respectively. Implementation of the EU's proposals on the two products that have yet to be genericized – Plavix (clopidogrel) and Crestor (rosuvastatin) – would increase costs for payers by approximately $2.8 billion.

As shown in Table 7, for these six products at least, patent term extensions have the largest effect on total costs. Since this is a small sample of cases, one should be careful about extrapolating that the other provisions are relatively unimportant – that would depend on the specifics of each product. A broader sample of the effects of the proposed CETA provisions is evident in Appendix III, featuring products genericized in 2010, many of which are primarily affected by extended data exclusivity and the right of appeal.

Table 8 shows that Ontario and Quebec would be most significantly affected by the EU proposals. The reason is that these provinces are large and that they have particularly large reductions in reimbursed prices following generic entry. The steep price reductions in these provinces is the result of pricing reforms by Ontario in 2010 (reducing generic prices from 50 percent to 25 percent of the brand price for public and private sector sales); Quebec is in the process of reducing generic prices to 25 percent of the brand price,[28] and BC and Alberta are implementing their own similar pricing reforms.

[28] We note that Quebec has a "15-year rule" which provides brand companies with 15 years following registration on the Quebec formulary during which the brand product is eligible for reimbursement at its full price. Despite this rule, when generic products are available at lower prices, prescriptions tend to be filled with the generic product, although at a lower utilization rate than in the rest of Canada.

TABLE 7: ESTIMATES OF ADDITIONAL SPENDING DUE TO THE PROPOSED CETA IP CHANGES, BY MOLECULE, IN MILLIONS OF DOLLARS

	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Norvasc (amlodipine)	720.8	0	0	**720.8**
Lipitor (atorvastatin)	1778.5	0	0	**1778.5**
Plavix (clopidogrel)	851.7	0	0	**851.7**
Reminyl ER (galantamine ER)	0	177.2	196	**196**
Altace (ramipril)	131.6	0	131.6	**131.6**
Crestor (rosuvastatin)	1922.3	545.3	365.4	**1922.3**
Total	**5404.9**	**722.5**	**693**	**5600.9**

TABLE 8: ESTIMATES OF ADDITIONAL SPENDING DUE TO THE PROPOSED CETA IP CHANGES, BY PROVINCE FOR THE SIX SELECTED MOLECULES, IN MILLIONS OF DOLLARS

PROVINCE	PATENT TERM EXTENSION (PTE)	EXTENDED DATA EXCLUSIVITY (EDE)	RIGHT TO APPEAL (RTA)	ALL
Alberta	414.7	51.8	50.3	**426.4**
British Columbia	431.2	54.9	60.9	**444.2**
Manitoba	183.7	16.8	15.8	**185.6**
NIHB	46.2	3.6	4.4	**46.2**
New Brunswick	98	15.8	15.7	**101.9**
Newfoundland and Labrador	79.5	14	11.5	**81**
Nova Scotia	119.1	20.1	18.5	**123.8**
Ontario	2291.3	348.3	342.9	**2416.8**
Prince Edward Island	9.6	1.4	1.4	**9.9**
Quebec	1584	177.1	154.4	**1615.4**
Saskatchewan	147.4	18.8	17.1	**149.4**
Total	**5,624.9**	**767.3**	**742.5**	**5,848.9**

It is worth noting that in estimating the total cost impact, cash-paying consumers who are excluded from IMS-Brogan data were not included. They may account for another one or two percent; and PEI's public plan was not included because sales data was not available from IMS Brogan. The territories are also excluded from this analysis.

The results also do not account for the importance of discounts paid by generic manufacturers to pharmacies in Canada. As is well known, in most Canadian jurisdictions generic manufacturers compete for sales by the payment of rebates, allowances, or other discounts to pharmacies. Pharmacies, in turn, argue that they use these rebates to keep dispensing fees low, given the level of service provided. A supplier that has exclusivity rights with respect to a drug does not need to compete to get its product into pharmacies and therefore does not pay such discounts to pharmacies. Although rebates in some public plans are being eliminated by the reduction in generic reimbursement prices, they likely are still paid for privately insured generic drug sales. There will therefore also be costs to pharmacies from the extension of exclusivity, which has not been calculated, in the absence of reliable information on the current and future scale of discounts.

Biologics

CETA's pharmaceutical IP provisions would affect not only small-molecule generic drugs but also follow-on versions of biological medicines. While biologic drugs have not been included in this analysis, biologics are becoming an increasingly important component in drug expenditures.

There are some complications in assessing how the EU's proposed language would apply to biologics, but the key effect is that it can be expected that exclusivity periods would likely increase for biologics, just as for small molecules. One important distinction is that competition from Subsequent Entry Biologics (the Canadian nomenclature for "generic" biologics) is likely to be relatively weak; the pioneer product is likely to retain market share leadership, and subsequent entry biologics are not likely to create very large price discounts. The effect is that extended exclusivity is not as financially important as in the case of small molecule drugs, where generics typically quickly dominate the market at large price discounts. However, because biologics will be the most expensive drugs in Canada, the lower percentage savings will still be substantial.

In March 2010, Health Canada issued a guidance document for sponsors of subsequent entry biologics, paving the way for follow-on competition for blockbuster biological medicines such as Epogen, Neupogen, Remicade and Humira. The brand versions of these products are currently used only exceptionally in Canada due to their very high cost.

Although it is hard to predict how the subsequent entry biologic market will develop, CETA's provisions would equally apply to biologics, lengthening the periods of market exclusivity by several years. Table 9 presents a brief summary of the patent term extension that would accrue for the five top-selling biologics over the next decade.

TABLE 9: PROJECTED PATENT TERM EXTENSIONS FOR IMPORTANT BIOLOGIC DRUGS

GENERIC NAME	BRAND NAME	GLOBAL SALES	PATENT	EXPIRY	PATENT TERM EXTENSION (PTE)
Infliximab	Remicade	$6.1 billion	2,106,299	Mar. 18, 2012	+ 4 years, 2 months, 18 days
Bevacizumab	Avastin	$5.9 billion	2,145,985	Oct. 28, 2012	+ 5 years
Rituximab	Rituxan	$5.8 billion	1,336,825	Aug. 29, 2012	+ 5 years
Adalimumab	Humira	$5.5 billion	2,243,459	Feb. 10, 2017	+ 2 years, 7 months, 14 days
Trastuzumab	Herceptin	$5.0 billion	1,341,082	Aug. 8, 2017	+ 5 years

As can be seen in Table 9, CETA would confer on each of the top biologics a substantial extension to exclusivity.

6. Impact on industry

Impact on brand manufacturers

The additional costs to drug plans from prolonged market exclusivity afforded to patented drugs represents additional revenues to brand drug companies. Thus, the EU's proposed IP provisions will increase brand drug company profits, assuming no significant countervailing responses by payers (such as additional limits on the set of drugs reimbursed or tougher price negotiations). Some of these profits will be used to fund the development of new drugs, which could create real benefits for Canadians and indeed residents of other countries.

The purpose of exclusivity rights granted to innovators is to create an incentive for research and development investment into new drugs. This paper does not take a position on the appropriate length of the exclusivity period afforded to new drugs. However, the effect of lengthened exclusivity in Canada on drug innovation globally and domestically can be examined.

Impact on Global Drug R&D

Assuming there is no countervailing response by payers, it is estimated that brand revenues would increase by approximately $4.6 billion per year if the EU proposals are implemented, calculated as follows:

Total Annual Brand Sales	$13.3 billion
x % Sales Going Generic	x 0.1
Annual Brand Sales Losing Exclusivity	$1.33 billion
x Number of Years Delay	x 3.46
Annual Incremental CETA Revenue	**$4.6 billion**

Approximately 15% of brand sales revenues are allocated to global drug R&D.[29] This implies that about $690 million of the $4.6 billion in additional brand company revenues would be allocated to R&D globally.

Annual Incremental CETA Revenue	**$4.6 billion**
x 15% Sales Devoted to Global R&D	x 0.15
Total Incremental Global R&D	**$690 million**

Impact on Domestic Drug R&D

There is frequently a significant industrial policy consideration to pharmaceutical IP policy. Canadian policy makers are concerned not only with the total amount of R&D activity, but also that this activity takes place within Canada. What impact will the EU proposals have on R&D spending in Canada?

[29] Weiss D, Naik P, Weiss R. The 'big pharma' dilemma: develop new drugs or promote existing ones? *Nature Reviews Drug Discovery* 2009; 8:533-534.

During the negotiations over the pharmaceutical IP policy reforms in the 1987, the brand name industry promised to spend 10% of sales revenues on R&D in Canada (Smith, 1993). In compliance with this agreement, this ratio rose to 12.9% in 1997. However, it has since fallen to 8.2% for Rx&D members, and 7.5% for all reporting pharmaceutical companies (Table 18, PMPRB, 2010). There is some evidence that this ratio may be falling further. According to a recent CBC report, Quebec's brand-name pharmaceutical industry has lost 1200 R&D jobs since 2008, when the sector had 2300 jobs.[30]

If the 7.5% ratio were to hold, we could anticipate that incremental brand revenues of $4.6 billion would result in additional R&D spending in Canada of approximately $345 million, about half the total global increase. This effect is calculated as follows:

Total Annual Brand Sales	$13.3 billion
x % Sales Going Generic	x 0.1
Annual Brand Sales Losing Exclusivity	$1.33 billion
x Number of Years Delay	x 3.46
Annual Incremental CETA Revenue	**$4.6 billion**
x 7.5% Sales Devoted to Domestic R&D	x 0.075
Total Incremental Domestic R&D	**$345 million**

Recall from Section 4 that the cost to Canadians of implementing the EU proposals would be approximately $2.8 billion per year, less than the $4.6bn in additional revenues to the brands, since the average price following generic entry would be about 61% less than the brand price.

Ignoring the effect on generic innovation, the EU proposals would thus require Canadians to spend $2.8 billion extra to obtain an additional $345 million of investment into pharmaceutical R&D in Canada. This represents approximately $8 of drug exclusivity premiums paid by Canadians to generate each additional $1 of domestic R&D.

$$\frac{\$2.8\ billion}{\$345\ million} \approx \frac{8}{1}$$

Whether the industry would unilaterally increase R&D spending in Canada is unclear. As noted above in Section 3, data exclusivity was extended from five years to eight in 2006. This has not resulted in any discernable increase in the amount of pharmaceutical R&D conducted in Canada. This suggests that other policy mechanisms could be more effective in achieving the objective of attracting increased pharmaceutical R&D spending. Specifically, if Canada wishes to increase its share of global pharmaceutical R&D expenditures, it would be better served to examine other options and initiatives that could enhance research productivity, such as ensuring an abundance of highly skilled researchers; establishing generous tax provisions; and supporting the development of

[30] "Quebec struggles to keep pharma R&D jobs." CBC News, 2 December 2010, http://www.cbc.ca/health/story/2010/12/01/que-government-increase-pharma-subsidies.html

universities with productive research portfolios in biopharmaceutical sciences.[31] Providing extended periods of monopoly protection applicable to all products, regardless of where the research is performed, is unlikely to be effective in shifting research to Canada.

Impact on generic manufacturers

R&D also occurs in the generic sector. According to PMPRB (2010), Rx&D members reported R&D expenditures of $1.1 billion in 2009. While R&D expenditures for the generic pharmaceutical industry in Canada are not reported annually by the PMPRB or other public sources, there is evidence that these investments are significant. According to RESEARCH Infosource Inc.'s annual list of Canada's Top 100 R&D Spenders, Toronto-based generic drug firm Apotex Inc. is the top R&D spender among all pharmaceutical/biotechnology companies in Canada. Apotex Inc. spent more than $188 million on R&D in 2009, or 15.9 percent of its domestic revenues on research and development. According to the same list of Top 100 R&D spenders, privately-held Montreal generic drug firm Pharmascience Inc. spent more than $30 million on R&D in 2009. The implication is that, to the extent we care about encouraging innovation in Canada, the generic industry is not insignificant compared to the branded pharmaceutical industry. It seems likely that generic company domestic R&D expenditures, which are mainly focused on formulation and production, will be more sensitive to changes in exclusivity periods than brand industry domestic R&D expenditures, which are largely devoted to clinical trials.

If Canada is one of the last jurisdictions in the world to allow generic market entry, generic companies in other countries will already have addressed the need for formulation and process engineering, and Canadian generic manufacturers will start off at a disadvantage in their own country. It can be anticipated that an increasing share of generic R&D will therefore be performed in countries with shorter exclusivity periods. It is possible that the net impact of increased exclusivity periods on total (brand and generic) pharmaceutical R&D conducted in Canada could even be negative.

Generic manufacturing in Canada and the export interests of generic companies will also be affected. In addition to production for the Canadian market, generic manufacturers also export drugs to more than 120 countries worldwide, according to information collected by CGPA. If exclusivity consistently ends later (or no earlier) in Canada than in the US, Mexico, and the EU, Canada will be an unattractive place to locate manufacturing plants, since Canadian plants will not be able to produce for export to those other markets before exclusivity ends in Canada. Generally, it can be anticipated

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[31] BIOTECanada has proposed a number of government policies to make Canada "a leading destination for knowledge industries like biotech," including: exempting investments in emerging tech companies from capital gains tax; reducing corporate taxes; increasing government funding to emerging tech companies; improving relevant educational opportunities; recruiting skilled immigrants; improving the regulatory framework for rapid development and approval of new technologies; and establishing "world leading intellectual property and data protection laws". Changing the intellectual property laws is only one of many ways to stimulate additional innovative investment in Canada. (*The Canadian Blueprint: Beyond Moose and Mountains*, available at www.beyondmooseandmountains.ca.)

that manufacturing of new products will start first in other countries, leading to a systematic disadvantage in generic manufacturing in Canada. There are global economies of scale in manufacturing – generic firm Teva Pharmaceutical Industry Ltd.'s regulatory submissions to the US Securities and Exchange Commission, for example, state that it believes it has advantages over rivals because its "global generic product infrastructure" gives it "the ability to concentrate production to achieve economies of scale." (Teva 2010, p. 30) The problem for the Canadian economy is that Canadian plants will not be able to supply globally for multinational corporations like Teva until Canadian exclusivity ends.

7. Impact on litigation costs

One of the important components of pharmaceutical expense in Canada is litigation, which costs hundreds of millions of dollars annually in the pharmaceutical industry. Most litigation is between generics and brands. Conservatively, the cost of litigating a NOC proceeding to its conclusion is $1-2 million per side, assuming that the proceeding runs smoothly.

The proposed changes to Canadian law will add to the amount of litigation and make NOC proceedings even more costly. First, enabling patentees to file NOC appeals will add another layer of litigation to many cases. It can be expected that the litigants will spend in the hundreds of thousands of dollars per appeal, though the expense will depend on the product and the legal issues at stake. Increased litigation costs will raise the profitability threshold required to develop a product for the Canadian market, leading generic companies to forego patent challenges for some smaller molecules.

Second, patent term extensions will inevitably be complex to determine, and this will create new litigation costs for generics, brands and the Federal government, which funds the relevant courts. In the EU, the complexities associated with supplementary protection certificates are leading to extensive litigation (Sheraton and Smith, 2010). Pharmaceutical companies in the United States also face significant litigation costs related to patent term extensions.

Third, merely changing laws creates new uncertainties as firms attempt to determine details of the implementation of new legislation and regulations. Of course, this does not mean that changes should never be contemplated: but it is important to verify that the benefits to the various stakeholders will be large enough to justify the changes.

Litigation carried on between brand and generic firms, of course, does not directly affect consumers. But the costs must inevitably be paid for, and it is ultimately payers who will fund any additional litigation.

8. Conclusion

The intellectual property language proposed by the EU in CETA would substantially increase the average time of exclusivity for patented drugs in Canada, and would give Canada the highest structural protection for patented drugs of any country in the world. While it is possible that this would enhance innovation incentives slightly, it is certain that it would increase the costs of purchasing drugs in Canada by billions of dollars annually. The estimated increased average annual cost to Canadians of implementing the EU's proposed language on pharmaceuticals is approximately $2.8 billion annually (assuming that insurers did not respond by reducing the set of drugs covered or by reducing prices paid). A significant share of this cost would be borne by provincial government health budgets, since provinces are the largest providers of drug insurance.

Several drugs were examined as case studies to explore how the impact of the EU's proposals would differ across provinces and products. The EU's proposals would have the effect of increasing costs to payers by hundreds of millions or even billions of dollars for each product.

Canada does, of course, have an obligation to support research into new drugs, not only through its international obligations under TRIPS and NAFTA, but also in a moral sense: Canada is a rich country, and should make a meaningful contribution to the costs of pharmaceutical innovation. The question, however, must be asked whether extensions of monopoly rights are the right way to achieve this goal: there are certainly other approaches that should be considered – such as directly sponsoring research through grants and tax incentives, or rewarding successful research on the basis of actual improvements in health through an institution such as the proposed Health Impact Fund, or establishing national support for drugs for rare diseases. If Canada wishes to increase its support for pharmaceutical innovation, there may be ways of achieving this goal that are more efficient, and less burdensome on government budgets, businesses and consumers than extending monopolies.

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Appendix I

This Appendix sets out in detail how each of the products evaluated in this report would be affected by the pharmaceutical IP provisions in CETA. The analysis in this Appendix, as well as Appendix III and V, was performed at our request by Gilbert's LLP.

In all cases, we have had to make assumptions about whether a product would be entitled to data exclusivity and/or a patent term extension. We have evaluated the eligibility of each drug for these extended protections based on (a) the plain text of the treaty, (b) the text of other trade agreements having comparable or contrasting language, and (c) EU and U.S. implementations of similar IP concepts, where relevant and applicable. These assumptions are based on current company behaviour. This study does not account for specific companies' change in behaviour to incorporate new strategies that maximize product lifecycles based on implementation of the CETA rules.

In brief, we have made the following assumptions to arrive at expected generic dates for each of the six molecules, as well as for the various molecules analysed in Appendix III:

Data Exclusivity

1. All pharmaceutical products which were approved according to a New Drug Submission (NDS) rather than a Supplementary New Drug Submission (SNDS) and differ from all existing pharmaceutical products in active ingredient, formulation (including strength or combination) or intended use would be entitled to data exclusivity.[32]

2. Products which were approved for an additional new indication within the first eight years of approval would be entitled to an additional year of data exclusivity.[33]

Patent Term Extension

3. Where multiple patents contain compound claims that could be construed to cover the active ingredient, all such patents could potentially be entitled to a patent term extension. This is consistent with US and EU law, which permits the brand company to select which patent covering the active ingredient it will seek to extend for a given product.[34]

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[32] This assumption accords with the language of the treaty, providing broad protection for "any information submitted to obtain an authorisation to put a pharmaceutical product on the market".

[33] Additional one-year data exclusivity is available for "one or more new therapeutic indications which are considered of significant clinical benefit in comparison with existing therapies". We are not privy to the clinical information submitted in respect of the additional indication. We have assumed that new clinical indications filed within the first eight years of approval would be of significant clinical benefit, absent any available information to the contrary.

[34] We have assumed that, if given the choice, brand companies will choose to extend the patent with the latest expiry date which is likely to be upheld in court. This may be a genus compound patent covering a broad class of compounds or a selection patent covering a subset of the genus compounds.

4. Patent term extensions are unavailable for invalid patents.

5. Salt, prodrug, ester and other patents containing chemical variations of existing active ingredients would be eligible for patent term extension. Combination patents and polymorph patents (for existing active ingredients) would not be eligible.

6. Six-month pediatric extension would be available in Canada if it was obtained in the U.S. under a similar provision involving scrutiny of the brand's pediatric studies.

7. For biologics listed in Appendix III, three products (Rituxan, Avastin and Herceptin) have multiple listed patents. We have conservatively assumed that patentees will most likely seek patent extensions on the listed patent having the earliest filing date, since this patent will generate the longest patent term extension and will normally be the least vulnerable to prior art challenges due to its early priority date.

Right of Appeal

8. No NOC proceeding would commence before eight years from the date of initial brand approval.

9. Where an NOC proceeding has already happened, the time to hearing has been incorporated into the delay calculations. Where no NOC proceeding has yet happened, we have assumed a time-to-hearing of 19.1 months, as calculated by Health Canada in respect of NOC proceedings commenced in 2007 (the latest reliable statistical evaluation). This latter assumption is conservative as it includes NOC proceedings which were resolved quickly by a court otherwise than on the merits.

10. Time from a hearing decision to an appeal decision is estimated to be one year. Although the time to appeal varies, an analysis of cases commenced since 2005 reveals an average delay from hearing to appeal of 372 days, or just over one year. A summary of the time-to-appeal for cases commenced since 2005 is contained in Appendix V.

Our assessment of the expected generic entry dates for each of the relevant molecules is set out below.

Atorvastatin (Lipitor®)

Atorvastatin, marketed by Pfizer as Lipitor, is the world's best-selling drug of all time, once eclipsing $13 billion in global sales. Atorvastatin is used widely to reduce cholesterol. During the last year of its patent protection term in Canada (2009), atorvastatin grossed Canadian sales exceeding $1.3 billion.

Atorvastatin went generic in Canada on May 19, 2010, with 10 generic manufacturers eventually receiving Health Canada authorisation to sell the product. Atorvastatin was immediately reimbursable across Canada at prices between 25 and 35 percent of the branded product.

As a result of several *PM(NOC)* proceedings primarily involving Ranbaxy and Apotex, generic entry was poised to occur on July 19, 2010 after expiry of Canadian Patent No. 2,021,546, a patent covering the specific enantiomer atorvastatin. Atorvastatin was also covered by an earlier compound patent until May 8, 2007, when Canadian Patent No. 1,268,768 expired. The 768 Patent had covered a large class of compounds that included atorvastatin.

Apart from the above two compound patents, generic companies were successful in challenging the remaining listed atorvastatin patents, of which there are currently 16 with expiry dates lasting until 2022.

Through a confidential settlement with Apotex, generic atorvastatin entry was achieved in Canada on May 29, 2010.[35]

Impact of CETA on Atorvastatin Entry Date

If the pharmaceutical IP provisions were in force in respect of atorvastatin and its patents, atorvastatin would have had 27 extra months of market exclusivity as the result of a patent term extension.

Under CETA, atorvastatin would be eligible for a patent term extension of nearly five years due to the delay between Pfizer's filing for the original compound patent (the 768 Patent) and approval of the Pfizer's atorvastatin product, Lipitor®. The patent application was filed on May 7, 1987, and the product was not approved until February 19, 1997. Under CETA, Pfizer would be entitled to a patent term extension equal to the delay between these two dates, less five years, up to a maximum of five years.

In addition, Lipitor would be entitled to a six-month pediatric exclusivity extension. Lipitor received such an extension in the United States for complying with the FDA's pediatric study requirement. We therefore assume that Pfizer's pediatric studies would also have qualified for a CETA pediatric extension.

The patent term extension and pediatric exclusivity extension for the 768 Patent would therefore expire on August 20, 2012, as follows:

768 Patent (Expiry Date)	**May 8, 2007**
Delay Period	+ 9 yrs, 9 mos, 12 days
Minus 5 years	- 5 yrs
768 Patent (Patent Term Extension)	**February 20, 2012**
Add 6-Month Pediatric Exclusivity	**August 20, 2012**

[35] "Lipitor generic reaches Canada, Pfizer vows fight", *Reuters Canada,* May 19, 2010, http://ca.reuters.com/article/businessNews/idCATRE64I64P20100519.

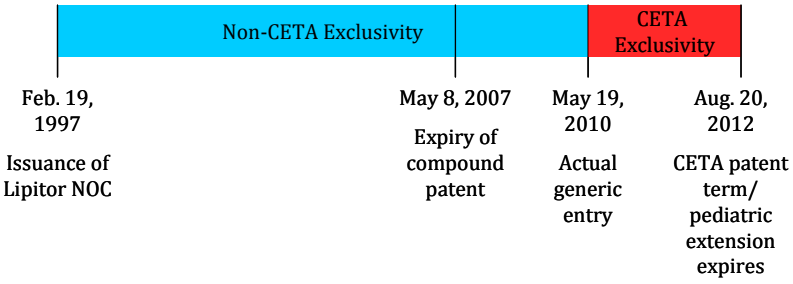
Atorvastatin entered the Canadian market on May 19, 2010. The effect of CETA would be to delay atorvastatin entry until August 20, 2012 – a delay of 27 months.

This added exclusivity period would result from the extension of the original compound patent, which had expired nearly five years prior, in 2007. This compound patent was upheld in *PM(NOC)* proceedings, and so there is no reason to believe that generics would be able to achieve entry any earlier than August 2012 under CETA.

Extended data exclusivity would not have a delaying effect for atorvastatin due to the extended patent protection for the drug. Under CETA, data exclusivity would expire on February 19, 2008, 11 years after issuance of Lipitor's original NOC. Lipitor would have been entitled to not only 10 years of exclusivity but also an additional one-year exclusivity for new indications relating to cholesterol and myocardial infarction added in 1999, 2002 and 2004, within eight years of Lipitor's initial approval.

Similarly, an appeal as of right from a negative *PM(NOC)* decision would likely not affect atorvastatin's entry date, as the trial court had granted the brand's application for a prohibition order for generic atorvastatin pending expiry of the 768 Patent.

The delayed entry of atorvastatin resulting from CETA is captured in the timeline below:



Amlodipine (Norvasc®)

Amlodipine, marketed by Pfizer as Norvasc, is a blockbuster anti-hypertensive drug used to treat angina. During the last year of its patent protection term (2008), amlodipine in Canada grossed sales of $485 million.

Amlodipine went generic in Canada on July 9, 2009, with 22 generic manufacturers eventually receiving Health Canada authorisation to sell the product. Entry resulted from a Federal Court trial decision impeaching Canadian Patent No. 1,321,393, a patent covering the besylate salt of amlodipine. The impeachment action had been launched by Ratiopharm after generic companies challenging the 393 Patent had lost their *PM(NOC)* applications (though they were successful in challenging other listed patents). Amlodipine had already gone generic in the United States in 2007.

After price negotiations between payers and generic companies, amlodipine was listed and reimbursable across Canada at prices between 35 and 50 percent of the branded product. Pfizer capitalized on Canadian demand for generic amlodipine by launching

its own authorised generic, by GenMed, and entering exclusivity agreements with payers for the product.

Without the impeachment action, amlodipine entry would have awaited expiry of the 393 Patent on August 17, 2010. Amlodipine had also previously been covered by a broad compound patent – Canadian Patent No. 1,253,865 – which expired on May 9, 2006.

Impact of CETA on Amlodipine Entry Date

If the pharmaceutical IP provisions were in force in respect of amlodipine and its patents, amlodipine would have had 28 extra months of market exclusivity as the result of a patent term extension.

Under CETA, amlodipine would be eligible for a patent term extension of five years due to the delay between Pfizer's filing for the original compound patent (the 865 Patent) and approval of the Pfizer's amlodipine product, Norvasc®. The application for the 865 Patent was filed on March 9, 1983, and the product was approved on August 1, 1997. Under CETA, Pfizer would be entitled to a patent term extension equal to the delay between these two dates, less five years, up to a maximum of five years.

In addition, Norvasc would be entitled to a six-month pediatric exclusivity extension. Norvasc received such an extension in the United States for complying with the FDA's pediatric study requirement. We therefore assume that Pfizer's pediatric studies would also have qualified for a CETA pediatric extension.

The patent term and pediatric exclusivity extensions for the 865 Patent would therefore expire on May 9, 2011, as follows:

865 Patent (Expiry Date)	**May 9, 2006**
Delay Period	+ 14 yrs, 7 mos, 23 days
Minus 5 years	- 5 yrs
865 Patent (Patent Term Extension)	**May 9, 2011 (5-year max)**
Add 6-Month Pediatric Exclusivity	**Nov. 9, 2011**

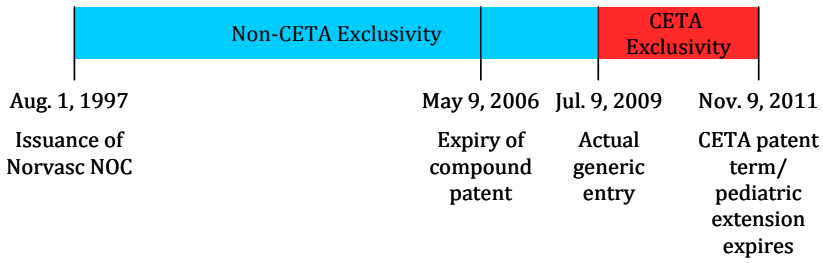
Amlodipine entered the Canadian market on July 9, 2009. The effect of CETA would be to delay amlodipine entry until November 9, 2011 – a delay of 28 months.

This added exclusivity period would result from the extension of the original compound patent, which had expired nearly five years prior, in 2006. This compound patent was upheld in *PM(NOC)* proceedings, and so there is no reason to believe that generics would be able to achieve entry any earlier than May 2011 under CETA, despite entry having been achieved four years earlier in the United States.

Extended data exclusivity would not have a delaying effect for amlodipine due to the extended patent protection for the drug. Under CETA, data exclusivity would expire on August 1, 2007, 10 years after issuance of Norvasc's original NOC.

Similarly, an appeal as of right from a negative *PM(NOC)* decision would not affect amlodipine's entry date, as the trial court had granted the brand's application for a prohibition order for generic amlodipine pending expiry of the 865 Patent, and the result in the 393 Patent impeachment action would not affect this finding.

The delayed entry of amlodipine resulting from CETA is captured in the timeline below:



Ramipril (Altace®)

Ramipril, marketed by Sanofi-Aventis as Altace, is an ACE inhibitor, used to treat hypertension and congestive heart failure. During the last year of its patent protection term (2006), ramipril grossed Canadian sales of $381 million.

Ramipril went generic on December 12, 2006, with Apotex entering the market after Health Canada determined that it did not need to address two of the patents listed on the Patent Register. Novopharm (now Teva) followed in May 2007, and there are now 14 generic manufacturers of ramipril in Canada.

Apart from patent barriers, Apotex' ramipril application was ready to be approved on April 26, 2004. The original compound patent had expired in May 2002, however there were six listed patents which needed to be addressed under the *PM(NOC) Regulations.* A prohibition order was issued in respect of Canadian Patent No. 1,246,457, a composition patent for treating cardiac insufficiency, until its expiry on December 13, 2005.

Apotex succeeded in overcoming three of the remaining five patents in *PM(NOC)* proceedings, with its final successful *PM(NOC)* trial decision rendered on June 27, 2006, holding invalid Canadian Patent No. 2,055,948, a patent for use of ramipril in combination with a calcium antagonist to treat proteinuria. On December 12, 2006, Health Canada determined that Apotex did not need to address two patents, to a new use, which were listed only after Apotex had filed its drug submission. Apotex entered the market the next day.

Impact of CETA on Ramipril Entry Date

If the pharmaceutical IP provisions were in force in respect of ramipril and its patents, ramipril would have likely had an extra year of additional market exclusivity as the result of a patent term extension, data exclusivity and/or appeal of *PM(NOC)* proceedings.

Under CETA, ramipril would be eligible for a patent term extension of five years due to the delay between Hoechst Marion Russell's (precursor to Sanofi-Aventis) filing for the original compound patent (the 087 Patent) and approval of Hoechst's ramipril product, Altace®. The patent application was filed on November 4, 1982, and the product was not approved until September 30, 1994. Under CETA, Pfizer would be entitled to a patent term extension equal to the delay between these two dates, less five years, up to a maximum of five years.

The patent term extension for the 087 Patent would therefore expire on May 14, 2007, as follows:

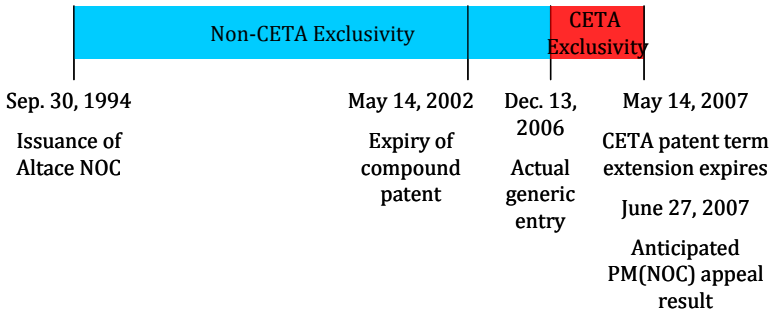
087 Patent (Expiry Date)	**May 14, 2002**
Delay Period	+ 11 yrs, 10 mos, 25 days
Minus 5 years	- 5 yrs
087 Patent (Patent Term Extension)	**May 14, 2007 (5-yr max)**

Additionally, if Sanofi-Aventis had been able to appeal the *PM(NOC)* decision involving the 948 Patent, then it could have prevented Apotex from receiving its NOC for several months, and possibly over a year, after the June 27, 2006 trial decision. Since the average length of time between hearing and appeal for NOC proceedings commenced since 2005 is approximately one year, a reasonable estimate of the delay from appeal would be one year – until June 27, 2007.

Generic ramipril entered the Canadian market on December 13, 2006. The effect of CETA would be to delay ramipril entry until June 27, 2007, and maybe longer.

Moreover, the only reason generic entry was not achieved on June 27, 2006 was that Health Canada had erroneously forced Apotex to address two late-listed patents, a decision which it reversed on December 12, 2006 as a result of a November 2006 Supreme Court of Canada decision. Had Apotex not been forced to address these two patents in the interim, then Apotex could have entered the market in June rather than December. In that case, the effect of CETA would be even more pronounced.

The delayed entry of ramipril resulting from CETA is captured in the timeline below:



Rosuvastatin (Crestor®)

Rosuvastatin, marketed by Astrazeneca as Crestor, is a statin used to reduce cholesterol. The drug's sales have been increasing rapidly – to $4.5 billion in global sales – in 2009, after clinical trials showed enhanced preventative benefits for the drug. Crestor is currently protected by patents in Canada, with no generic competition.

Several companies have outstanding *PM(NOC)* proceedings in respect of rosuvastatin. The proceedings pertain to two patents – Canadian Patent Nos. 2,072,945 and 2,313,783. Teva, Sandoz and Ratiopharm have successfully challenged the 783 Patent, and others are awaiting hearing dates in November 2010 (Cobalt), April 2011 (Sandoz) and April 2012 (Teva and Apotex) in respect of the 945 Patent. The 945 Patent expires on July 2, 2012.

Impact of CETA on Rosuvastatin Entry Date

If the pharmaceutical IP provisions were in force in respect of rosuvastatin and its patents, rosuvastatin will likely gain an additional 5.5 years of market exclusivity as the result of a patent term extension, pediatric extension, extended data exclusivity and/or an added right of appeal from a negative *PM(NOC)* decision.

Under CETA, rosuvastatin would be eligible for a patent term extension of five years due to the delay between Astrazeneca's filing for the original compound patent (the 945 Patent) and approval of Astrazeneca's rosuvastatin product, Crestor®. The patent application was filed on July 2, 1992, and the product was not approved until February 16, 2003. Under CETA, Astrazeneca would be entitled to a patent term extension equal to the delay between these two dates, less five years, up to a maximum of five years.

In addition, Crestor would be entitled to a six-month pediatric exclusivity extension. Crestor received such an extension in the United States for complying with the FDA's pediatric study requirement. We therefore assume that Astrazeneca's pediatric studies would also have qualified for a CETA pediatric extension.

The patent term and pediatric exclusivity extensions for the 945 Patent would therefore expire on January 2, 2018, as follows:

945 Patent (Expiry Date)	**July 2, 2012**
Delay Period	+ 10 yrs, 7 mos, 14 days
Minus 5 years	- 5 yrs
945 Patent (Patent Term Extension)	**July 2, 2017 (5-yr max)**
Add 6-Month Pediatric Exclusivity	**Jan. 2, 2018**

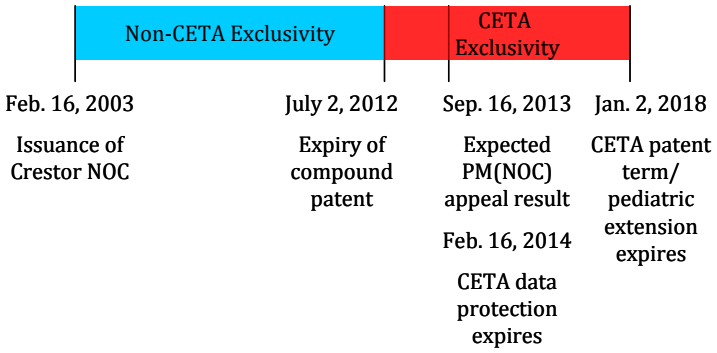
Additionally, Crestor® would benefit from data exclusivity for 11 years from the date of its initial NOC. In addition to 10 years of data exclusivity, Crestor would obtain an additional one-year exclusivity for a new indication added in 2010 for use in preventing myocardial infarction and stroke. Since the product was approved on February 16, 2003, data exclusivity would last until February 16, 2014.

Furthermore, no generic rosuvastatin application could be submitted until eight years from Astrazeneca's NOC – February 16, 2011. (Teva's *PM(NOC)* proceeding for generic rosuvastatin commenced on October 23, 2008, suggesting that its submission was filed approximately 45 days earlier, on September 8, 2008. The filing of Teva's application would therefore have been delayed by nearly 2.5 years.)

If Astrazeneca was entitled to appeal a negative *PM(NOC)* decision, it could delay generic entry even further. In the case of rosuvastatin, suppose the 945 Patent was held invalid in a *PM(NOC)* decision 24 months from the filing of the first *PM(NOC)* application, on February 16, 2013. If the brand could appeal this decision, it could delay entry by several months, and possibly over a year. Health Canada has calculated average time to an NOC decision at 19.1 months, and we have calculated average time from an NOC decision to appeal decision to be one year. Accordingly, a brand appeal of a negative decision would be estimated to take approximately 31 months to complete. This would extend exclusivity on Crestor until September 16, 2013.

Regardless of whether the 945 Patent is valid, CETA would cause generic entry of rosuvastatin to be delayed well beyond the current patent-off date of July 2, 2012.

The delayed entry of rosuvastatin resulting from CETA is captured in the timeline below:



Clopidogrel (Plavix®)

Clopidogrel, marketed by Sanofi-Aventis as Plavix, is an anti-platelet agent used to inhibit blood clots in heart disease. It had global sales of $6.6 billion in 2009, despite being genericized in India and for a brief time in the United States. Clopidogrel remains on-patent in Canada, with no generic competition, as a result of a Supreme Court of Canada decision upholding Canadian Patent No. 1,336,777.

Four generic companies (Teva, Apotex, Cobalt and Pharmascience) have commenced proceedings in respect of clopidogrel, and are awaiting expiry of the 777 Patent on August 22, 2012 so they may enter the clopidogrel market. An earlier patent covering a broad class of compounds including clopidogrel – Canadian Patent No. 1,194,875 – expired in 2002, before commencement of the *PM(NOC)* proceedings.

Impact of CETA on Clopidogrel Entry Date

If the pharmaceutical IP provisions were in force in respect of clopidogrel and its patents, clopidogrel could gain an additional five years of market exclusivity as the result of a patent term extension.

CETA is unclear regarding which patent covering a drug is eligible to be extended. Although racemic clopidogrel is covered by the earlier-expiring 875 Patent, the actual enantiomeric drug in its marketed salt form – is covered specifically in the 777 Patent. Suppose Sanofi-Aventis was eligible for a patent term extension of the 777 Patent due to the delay between Astrazeneca's filing for the 777 Patent and approval of the Sanofi-Aventis's clopidogrel product, Plavix®. The patent application was filed on February 8, 1988, and the product was not approved until October 7, 1998. Under CETA, Sanofi-Aventis would be entitled to a patent term extension equal to the delay between these two dates, less five years, up to a maximum of five years.

In addition, Plavix would be entitled to a six-month pediatric exclusivity extension. Plavix recently received such an extension in the United States for complying with the FDA's pediatric study requirement. We therefore assume that Sanofi-Aventis' pediatric studies would also have qualified for a CETA pediatric extension.

The patent term and pediatric exclusivity extensions for the 777 Patent would therefore expire on February 22, 2018, as follows:

777 Patent (Expiry Date)	**August 22, 2012**
Delay Period	+ 10 yrs, 7 mos, 29 days
Minus 5 years	- 5 yrs
777 Patent (Patent Term Extension)	**August 22, 2017 (5-yr max)**
Add 6-Month Pediatric Exclusivity	**Feb. 22, 2018**

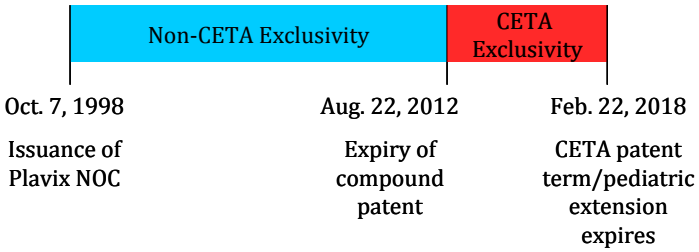
Generic clopidogrel is poised to enter the Canadian market on August 22, 2012. The effect of CETA would be to delay clopidogrel entry until February 22, 2018 – a delay of 5.5 years.

This added exclusivity period would result from the extension of the dedicated clopidogrel patent, which is set to expire in 2012. This patent was upheld in *PM(NOC)* proceedings at the Supreme Court level, and so there is no reason to believe that generics would be able to achieve entry any earlier than February 2018 under CETA, despite entry being expected in 2012 in the United States.

Extended data exclusivity would not have a delaying effect for clopidogrel due to the extended patent protection for the drug. Under CETA, data exclusivity would expire on October 7, 2009, 11 years after issuance of Plavix's original NOC. Plavix would have been entitled to not only 10-year exclusivity but also an additional one-year exclusivity for a new indication relating to atherothrombotic events added in 2002, within eight years of Plavix's initial approval.

Similarly, an appeal as of right from a negative *PM(NOC)* decision would not affect clopidogrel's entry date, as the trial court had granted the brand's application for a prohibition order for generic clopidogrel pending expiry of the 777 Patent.

The delayed entry of clopidogrel resulting from CETA is captured in the timeline below:



Galantamine Extended Release (Reminyl ER®)

Galantamine extended release (ER), marketed by Janssen-Ortho as Reminyl ER, is a cholinterase inhibitor, used to treat Alzheimer's disease. Reminyl ER was first marketed on April 8, 2005, and in 2010, Janssen enjoyed global Reminyl ER sales of approximately $64 million.

Reminyl ER went generic in Canada on November 12, 2010, with Mylan receiving a NOC after a successful *PM(NOC)* proceeding challenging Canadian Patent No. 2,310,950, a patent directed at a dosage regimen for administering galantamine to Alzheimer's patients. The 950 Patent does not expire until June 27, 2020. Mylan is the only generic manufacturer of galantamine ER on the market.

Galantamine ER is a follow-on product of a normal-release galantamine product marketed by Janssen as REMINYL. There is no compound patent covering galantamine, since the compound was discovered in the 1950s, long before the products were marketed.

Impact of CETA on Galantamine ER Entry Date

If the pharmaceutical IP provisions were in force in respect of galantamine ER and its patents, galantamine ER would have had approximately five years of additional market exclusivity as the result of data exclusivity and/or appeal of *PM(NOC)* proceedings.

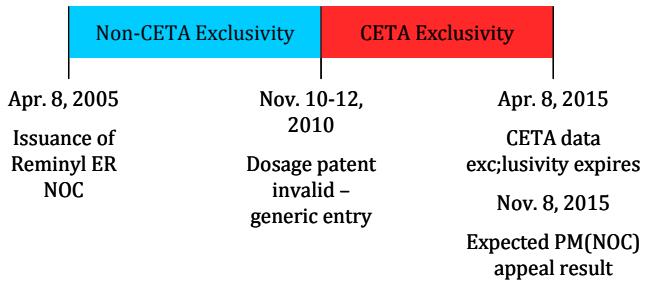
Since galantamine ER contains a previously-approved medicinal ingredient (galantamine), Health Canada would not grant Reminyl ER data exclusivity under the current data exclusivity regime. The current regime is limited only to "innovative drugs", specifically excluding drugs that contains previously-approved medicinal ingredients and their variations.

However, CETA requires that Canada confer 10 years of data exclusivity on all pharmaceutical products, regardless of their similarity to an existing product. This means that Reminyl ER would have been entitled to 10 years of protection from the date of issuance of its NOC. Since Janssen's initial Reminyl ER NOC was issued on April 8, 2005, the data exclusivity term would expire on April 8, 2015. This would have extended Janssen's exclusivity for galantamine ER by over four years.

Additionally, Janssen was unsuccessful in its *PM(NOC)* proceeding against Mylan, with judgment rendered against Janssen on November 10, 2010. If CETA were enacted, Mylan's *PM(NOC)* application could not have started until eight years from Janssen's NOC, or April 8, 2013. After Mylan's success at first instance, Janssen would likely have appealed (as it has attempted to do even under the current regime), delaying issuance of Mylan's NOC by an estimated one year. The combined effect of Mylan's delayed generic filing and *PM(NOC)* appeal would likely cause generic competition to accrue even later than expiry of Janssen's data exclusivity. Compounded with Health Canada's 19-month estimated time to an NOC hearing decision, the NOC appeal would have extended Janssen's exclusivity until Nov. 8, 2015

CETA's patent term extension provision would not play a role for Reminyl ER, as there are no patents directed at the galantamine compound, whether in normal release or ER form.

The delayed entry of galantamine ER resulting from CETA is captured in the timeline below:



Appendix II

This Appendix provides the methodology for the calculations in Table 3. We abstracted data on projected 2010 public and private drug expenditures by province from the CIHI 2010 report, Tables D.3 and D.1.

We scaled private expenditures down by 26.5% to account for the national level of private expenditures on non-prescription drugs. These are measures of total drug spending, which we assumed were proportional with spending on branded drugs.

We then scaled drug expenditures to account for the savings rates we anticipate will be achieved by different payers given generic availability. Specifically, we assumed that the average price reduction following generic entry would be 65% of the pre-generic brand price in Ontario and Quebec; 55% in British Columbia, Saskatchewan and Manitoba; and 50% in all other jurisdictions. While on average generic price reductions are expected to be larger than this, these rates also allow for some branded product to continue to be sold at the original high price.

These discount rates were multiplied by our measures of total prescription drug spending by sector and province. Normalizing by the sum, this provided a weighting for the allocation of the projected savings of $2.8 billion across provinces and sectors.

Appendix III

Chart Representation of CETA Delay Information

We have evaluated the effect of CETA's IP provisions on the six selected molecules of interest, as well as molecules that were first genericized in 2010. We have also evaluated patent extension information for the top five biologics products, set to go off-patent later this decade. Our delay analysis for all products is captured in the chart below:

6 EXAMPLES

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
LIPITOR (Atorvastatin)	May 19, 2010	Initial NOC approved Feb. 19, 1997 8 years ends Feb. 19, 2005 10 years ends Feb. 19, 2007 Add 1 year for new indications within 8 years of initial approval(1999 cholesterol, 2002 cholesterol, 2004 myocardial infarction) Exclusivity ends Feb. 19, 2008 Exclusivity would have expired before generic entry	Compound patent 1,268,768 expired on May 8, 2007 Enantiomer & salt selection patent 2,021,546 expired on July 19, 2010 Apotex won NOC proceeding on 546 Patent on Jan. 4, 2008 (2008 FC 13) but did not enter until May 19, 2010 Case decided nearly 3 years after 8-year data exclusivity, and no appeal → expect no effect from right of appeal	Last unexpired patent not held invalid against all generics was CP 1,268,768, which expired on May 8, 2007 768 Patent was filed May 7, 1987 Delay until approval was 9 years, 9 months, 12 days Subtract 5 years: PTE is 4 years, 9 months, 12 days Extension of 768 Patent leads to exclusivity expiry of February 20, 2012 Pediatric exclusivity granted in US for pediatric studies – therefore add 6 months exclusivity → **August 20, 2012**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
NORVASC (Amlodipine)	July 9, 2009	Initial NOC approved Aug. 1, 1997 8 years ends Aug. 1, 2005 10 years ends Aug. 1, 2007 Do not add 1 year for new indications – old indication updated in 2005 (within 8 years) is not new indication Exclusivity ends Aug. 1, 2007 Exclusivity would have expired before generic entry	Generics failed in NOC proceedings, so no appeal necessary for brand Generic entry resulted from generic impeachment action of salt selection patent 1,321,393 No delay in generic amlodipine entry if brands afforded right of NOC appeal	Last unexpired patent not held invalid was compound patent 1,253,865, which expired on May 9, 2006 865 Patent was filed on Mar. 9, 1983 Delay until approval was 14 years, 7 months, 23 days PTE is 5 years – maximum allowed under CETA Extension of 865 Patent leads to exclusivity expiry of May 9, 2011 Pediatric exclusivity granted in US for pediatric studies – therefore add 6 months exclusivity → **November 9, 2011**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
ALTACE (Ramipril)	December 12, 2006	Initial NOC approved September 30, 1994 8 years ends Sep. 30, 2002 10 years ends Sep. 30, 2004 Add 1 year for new indication in 2001 (cardiovascular events) Exclusivity ends Sep. 30, 2005 Exclusivity would have expired before generic entry	Apotex won in NOC proceedings on June 27, 2006 (had already received tentative approval on Apr. 26, 2004) Entry did not occur until Dec. 12, 2006 due to Health Canada delay in deciding Apotex didn't have to address 2 of listed patents In infringement action, Court held compound patent 1,341,206 invalid NOC appeal would have taken estimated 1 year to resolve Final decision permitting generic entry likely to occur on **June 27, 2007**	Since 206 Patent held invalid, last unexpired patent not held invalid was compound patent 1,187,087, which expired on May 14, 2002 087 Patent was filed on Nov. 4, 1982 Delay until approval was 11 years, 10 months, 25 days PTE is 5 years – maximum allowed under CETA Extension of 087 Patent leads to exclusivity expiry of **May 14, 2007** No pediatric studies/exclusivity conducted in US, so assume no pediatric extension in Canada

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
CRESTOR (Rosuvastatin)	Expected: July 3, 2012 (after expiry of compound patent 2,072,945)	Initial NOC approved on Feb. 16, 2003 8 years ends Feb. 16, 2011 10 years ends Feb. 16, 2013 Add 1 year for new indication in 2010 (preventative for myocardial/stroke) Exclusivity ends **Feb. 16, 2014**	No NOC hearing yet on 945 Patent – various hearings scheduled between Dec. 2010 and Apr. 2012 NOC appeal right would only matter if 945 Patent held invalid (yet to be seen) If parties were prevented from filing NOC proceedings until Feb. 16, 2011 and proceeding lasted 19 months to hearing decision and 1 year to appeal decision, NOC appeal on 945 Patent could lead to stay of approval until **Sep. 16, 2013**	Last unexpired patent not held invalid is 945 Patent, which expires on Jul. 2, 2012 945 Patent was filed on Jul. 2, 1992 Delay until approval was 10 years, 7 months, 14 days PTE is 5 years – maximum allowed under CETA Extension of 945 Patent leads to exclusivity expiry of Jul. 2, 2017 Pediatric exclusivity granted in US for pediatric studies – therefore add 6 months exclusivity → **Jan. 2, 2018**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
PLAVIX (Clopidogrel)	Expected: Aug. 23, 2012 (after expiry of enantiomer selection patent 1,336,777)	Initial NOC approved on Oct. 7, 1998 8 years ends Oct. 7, 2006 10 years ends Oct. 7, 2008 Add 1 year for new indication in 2002 (atherothrombotic events) Exclusivity ends Oct. 7, 2009 Exclusivity would have expired before generic entry	Brand won NOC proceedings on 777 Patent, and generic appealed to Supreme Court and lost NOC appeal for brand would have no effect on timing of generic entry	Last unexpired patent not held invalid is 777 Patent, which expires on Aug. 22, 2012 777 Patent was filed on Feb. 8, 1988 Delay until approval was 10 years, 7 months, 29 days PTE is 5 years – maximum allowed under CETA Extension of 777 Patent leads to exclusivity expiry of Aug. 22, 2017 Pediatric exclusivity granted in US for pediatric studies – therefore add 6 months exclusivity → **Feb. 22, 2018**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
REMINYL ER (Galantamine ER)	Nov. 12, 2010	Assume different from non-ER REMINYL due to extended release formulation Initial NOC approved on Apr. 8, 2005 8 years ends on Apr. 8, 2013 10 years ends on Apr. 8, 2015 No new indications Exclusivity would end on **Apr. 8, 2015**	Mylan won NOC proceeding on Nov. 10, 2010 in respect of dosage regimen patent 2,310,950 If parties were prevented from filing NOC proceedings until Apr. 8, 2013 and proceeding lasted 19 months to hearing decision and 1 year to appeal decision, NOC appeal on 950 Patent could lead to stay of approval until **Nov. 8, 2015**	Compound discovered in 1950s, use patent invalidated in U.S. Patents on Patent Register do not cover galantamine or its approved use in treatment of Alzheimer's (previously patented); patents cover neuropsychiatric behaviour associated with Alzheimer's (926 Patent); recommended dosage regimens (950 Patent); and a controlled release formulation (062 Patent) – none of listed patents eligible for patent term extension Patent term extension unavailable for galantamine ER

2010 EXAMPLES

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
ACTONEL (Risedronate)	Jan. 27, 2010	Initial NOC approved on Aug. 18, 1999 8 years ends Aug. 18, 2007 10 years ends Aug. 18, 2009 Add 1 year for new indication in 2000, 2001, 2006 Exclusivity ends **Aug. 18, 2010**	Brands were successful in NOC proceedings NOC appeal for brand would have no effect on generic entry	Last unexpired patent not held invalid is compound and composition patent 1,320,727, which expired on Jul. 27, 2010 727 Patent was filed on Dec. 19, 1985 Delay until approval was 13 years, 7 months, 30 days PTE is 5 years – maximum allowed under CETA Extension of 727 Patent leads to exclusivity expiry of Jul. 27, 2015 Pediatric exclusivity granted in US for pediatric studies – therefore add 6 months exclusivity → **Jan. 27, 2016**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
PROSCAR (Finasteride)	Jan. 29, 2010	Initial NOC approved Oct. 23, 1992 Exclusivity would have expired well before generic entry (2002)	Generics (Sandoz, Pharmascience) were successful in NOC proceeding on May 11, 2010, but entry occurred before NOC decision Given early entry, unclear whether NOC appeal would have prevented generic entry Assuming generic would have been prevented from entering until final appellate decision, entry would not have been likely for over 15 additional months, until **May 11, 2011**	Last unexpired patent not held invalid is compound patent 1,314,541, which expired on Mar. 16, 2010 541 Patent was filed on Feb. 26, 1985 Delay until approval is 7 years, 7 months 25 days PTE is 2 years, 7 months, 25 days Extension of 541 Patent leads to exclusivity expiry of **Nov. 11, 2012**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
ALTACE HCT (Ramipril HCTZ)	Feb. 2, 2010	Initial NOC approved on Jul. 13, 2006 8 years ends Jul. 13, 2014 10 years ends Jul. 13, 2016 No new indications Exclusivity ends **Jul. 13, 2016**	NOC proceedings for this molecule were discontinued on Jan. 8, 2010, therefore assume that NOC appeal for brand would have no effect	None of listed patents cover compound; as set out in Appendix I, patent term extension for ramipril compound patent would terminate in May 2007 None of listed patents could be extended beyond 2015 due to latest expiry date in 2010

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
COSOPT (Dorzolamide / timolol) * In view of unpredictability in PTE and NOC proceeding outcomes, we assume very conservatively that there would be no delay from CETA's proposed provisions	Feb. 12, 2010	Initial NOC approved on May 10, 1999 8 years ends May 10, 2007 10 years ends May 10, 2009 No new indications Exclusivity ends Oct. 7, 2009 Exclusivity would have expired before generic entry	NOC proceedings involving Sandoz for this molecule were discontinued on Dec. 15, 2009, therefore assume that NOC appeal for brand would have no effect Merck pursued NOC proceedings against Apotex, which were heard in August 2010 and dismissed on October 22, 2010 Given Merck's different approaches in NOC proceedings, unclear whether NOC appeal would have prevented generic entry Could assume generic would have been prevented from entering until final appellate decision, in which case entry would not have been likely for 12 additional months after NOC decision Since cross-examinations were incomplete and no hearing date had been set in the Sandoz proceeding, assume Apotex proceeding would have been heard first – 12 months from Apotex NOC decision is **Oct. 22, 2011**	Last unexpired patent not held invalid is compound patent 1,328,262, which would have expired on Apr. 5, 2011 262 Patent did not prevent generic entry as it was dedicated to the public by Merck in 2007; Merck alleged that this dedication cured Canadian Patent No. 1,329,211 from a double-patenting allegation It is unclear whether and how Merck would have asserted the 262 and 211 Patents if patent term extensions were available Could assume Merck would extend 262 Patent due to earlier filing date and easier avoidance of double-patenting allegation 262 Patent was filed on June 23, 1988 Delay until approval was 10 years, 10 months, 18 days PTE could be 5 years – maximum allowed under CETA Extension of 262 Patent would lead to exclusivity expiry of **Apr. 5, 2016**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
FEMARA (Letrozole)	Apr. 7, 2010	Initial NOC approved on May 21, 1997 8 years ends May 21, 2005 10 years ends May 21, 2007 Add 1 year for new indications in 2001, 2005 April Exclusivity ends May 21, 2008 Exclusivity would have expired before generic entry	No NOC proceedings for this molecule, therefore NOC appeal for brand would have no effect	Last unexpired patent not held invalid is compound patent 1,316,928, which expired on Apr. 27, 2010 Despite regulatory approval, no generic company launched prior to expiry of the 928 Patent 928 Patent was filed on Mar. 5, 1987 Delay until approval is 10 years, 2 months 16 days PTE is 5 years – maximum allowed under CETA Extension of 928 Patent leads to exclusivity expiry of **April 27, 2015**
LIPITOR (Atorvastatin)	May 19, 2010	See above	See above	See above

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
PRIMAXIN (Cilastatin Sodium/ Imipenem)	May 20, 2010	Initial NOC approved August 8, 2005 8 years ends Aug. 8, 2013 10 years ends Aug. 8, 2015 No new indications Exclusivity would end on **Aug. 8, 2015**	No NOC proceedings for this molecule, therefore NOC appeal for brand would have no effect	No relevant patents to extend

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
REVATIO (Sildenafil)	June 8, 2010	Assume REVATIO is new product, different from VIAGRA (different dosage and use) Initial NOC approved on May 26, 2006 8 years ends May 26, 2014 10 years ends May 26, 2016 No new indications Exclusivity ends **May 26, 2016**	Ratiopharm won NOC proceeding on June 8, 2010 in respect of use patent 2,324,324 NOC appeal would have taken estimated 1 year to resolve Final decision permitting generic entry likely to occur on approximately **June 8, 2011**	No relevant patents to extend Compound patent 2,044,748 was held not soundly predicted Use patent 2,163,446 for impotence (upheld in court) does not relate to REVATIO use Use patent 2,324,324 was held invalid in REVATIO NOC proceedings
GLUCONORM (Repaglinide)	Jul. 26, 2010	Initial NOC approved on Apr. 6, 1999 8 years ends Apr. 6, 2007 10 years ends Apr. 6, 2009 Add 1 year for new indication in 2005 Exclusivity ends Apr. 6, 2010 Exclusivity would have expired before generic entry	Cobalt won NOC proceeding on July 15, 2010 in respect of use patent 2,111,851 NOC appeal would have taken estimated 1 year to resolve Final decision permitting generic entry likely to occur on approximately **July 15, 2011**	Compound patent 1,225,398 not relevant since patent extension could not go beyond 2009 (after 2004 expiry) 1,292,000 Patent is a polymorph patent, not likely eligible for patent term extension

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
ACTONEL plus CALCIUM (Risedronate sodium/calcium carbonate)	Jul. 28, 2010	Initial NOC approved on May 17, 2006 8 years ends May 17, 2014 10 years ends May 17, 2016 No new indications Exclusivity ends **May 17, 2016**	NOC proceedings for this molecule were discontinued on Apr. 14, 2009, therefore assume that NOC appeal for brand would have no effect	Assume risedronate patents block entry on risedronate/ calcium: Last unexpired patent not held invalid is compound and composition patent 1,320,727, which expired on Jul. 27, 2010 727 Patent was filed on Dec. 19, 1985 Delay until approval was 13 years, 7 months, 30 days PTE is 5 years – maximum allowed under CETA Extension of 727 Patent leads to exclusivity expiry of **Jul. 27, 2015**

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
STRATTERA (Atomoxetine)	Sep. 16, 2010	Initial NOC approved on Dec. 24, 2004 8 years ends Dec. 24, 2012 10 years ends Dec. 24, 2014 No new indications Exclusivity ends **Dec. 24, 2014**	Although Apotex challenged Canadian Patent No. 2,209,735 in a NOC proceeding, Teva challenged the same patent successfully in an impeachment proceeding heard at the same time and entered the market NOC appeal by Apotex would not affect Teva's market entry	Use patent 2,209,735 was invalidated – therefore no patent term extension Earlier patent 1,181,430 expired several years ago in 2002, rendering patent term extension irrelevant
DIOVAN (Valsartan) * excluded from analysis[36]	Oct. 8, 2010	Initial NOC approved on Nov. 3, 1997 8 years ends Nov. 3, 2005 10 years ends Nov. 3, 2007 Add 1 year for new indication in Sep 2005 Exclusivity ends Nov. 3, 2008 Exclusivity would have expired before generic entry	No NOC proceedings for this molecule, therefore NOC appeal for brand would have no effect	Compound patent 2,036,427 was not challenged and expires on Feb. 15, 2011 427 Patent was filed on Feb. 15, 1991 Delay until approval was 6 years, 8 months, 19 days PTE is 1 year, 8 months, 19 days Had this product been included in analysis, extension of 427 Patent would have led to exclusivity expiry of **Dec. 4, 2012**

[36] The generic entrant for valsartan (DIOVAN) was Sandoz, a subsidiary of the brand company, Novartis. Despite receiving regulatory approval, Sandoz has not launched its product. Since this product was not available to consumers during 2010, this product has been excluded from the calculation of average delay caused by CETA associated with molecules genericized in 2010.

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
CESAMET (Nabilone)	Nov. 1, 2010	Initial NOC approved on Apr. 20, 2000 8 years ends Apr. 20, 2008 10 years ends Apr. 20, 2010 No new indications Exclusivity ends Apr. 20, 2010 Exclusivity would have expired before generic entry	No NOC proceedings for this molecule, therefore NOC appeal for brand would have no effect	No relevant patents to extend
REMINYL ER (Galantamine ER)	Nov. 12, 2010	See above	See above	See above

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
VIRAMUNE (Nevirapine)	Nov. 16, 2010	Initial NOC approved on Sep. 4, 1998 8 years ends Sep. 4, 2006 10 years ends Sep. 4, 2008 No new indications Exclusivity ends Sep. 4, 2008 Exclusivity would have expired before generic entry	No NOC proceedings for this molecule, therefore NOC appeal for brand would have no effect	No relevant patents to extend

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
AVANDAMET (Rosiglitazone/ Metformin) * Since 452 Patent not asserted against this product, we assume very conservatively that a PTE for the 452 Patent would not be sought	December 21, 2010	Initial NOC approved February 13, 2003 8 years ends Feb. 13, 2011 10 years ends Feb. 13, 2013 No new indications Exclusivity would end on **Feb. 13, 2013**	No NOC proceedings for this molecule (although proceedings are ongoing for related rosiglitazone product, AVANDIA) – conservatively assume that NOC appeal for brand would have no effect	Although three patents are listed on the Patent Register, none were asserted in respect of generic rosiglitazone/metformin Compound patent 1,328,452, relating to rosiglitazone, is in ongoing PM(NOC) litigation in relation to AVANDIA Could assume GSK would extend 452 Patent since it has been asserted against a related product, but PTE may apply only to extend rosiglitazone-only product (since PTE is calculated based on "first authorisation" of the relevant product) 452 Patent was filed on Sep. 2, 1988 Delay until approval of first rosiglitazone product (AVANDIA, approved on Mar. 21, 2000) was 11 years, 6 months, 19 days PTE could be 5 years – maximum allowed under CETA Extension of 452 Patent would lead to exclusivity expiry of **April 12, 2016**

BIOLOGICS

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
REMICADE (Infliximab)	Unknown	Not assessed	Not assessed	Compound patent 2,106,299 expires on Mar. 18, 2012 Delay until approval was 9 yrs, 2 mo, 18 days PTE is 4 yrs, 2 mo, 18 days Extension of 299 Patent leads to exclusivity expiry of Jul. 27, 2015
AVASTIN (Bevacizumab)	Unknown	Not assessed	Not assessed	Compound patent 2,145,985 expires on Oct. 28, 2012 Delay until approval was over 10 years PTE is 5 years – maximum allowed under CETA Extension of 985 Patent leads to exclusivity expiry of Oct. 28, 2017

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
RITUXAN (Rituximab)	Unknown	Not assessed	Not assessed	Compound patent 1,336,826 expires on Aug. 29, 2012 Delay until approval was over 10 years PTE is 5 years – maximum allowed under CETA Extension of 825 Patent leads to exclusivity expiry of Aug. 29, 2017
HUMIRA (Adalimumab)	Unknown	Not assessed	Not assessed	Compound patent 2,243,459 expires on Feb. 10, 2017 Delay until approval was 7 yrs, 7 mo, 14 days PTE is 2 years, 7 months, 14 days Extension of 459 Patent leads to exclusivity expiry of Sep. 24, 2019

DRUG	GENERIC ENTRY DATE	DATA EXCLUSIVITY	NOC APPEAL	PATENT TERM EXTENSION
HERCEPTIN (Trastuzumab)	Unknown	Not assessed	Not assessed	Compound patent 1,341,082 expires on Aug. 8, 2017 Delay until approval was over 10 years PTE is 5 yrs – maximum allowed under CETA Extension of 082 Patent leads to exclusivity expiry of Aug. 8, 2022

Appendix IV: Assumptions of the average reimbursed price ratio *d* following generic entry

Quarter following generic entry	AB	BC	MB	NB	NIHB	NL	NL	NS	ON	PE	QC	SK
1	70	70	70	70	70	70	70	70	60	70	60	70
2	65	60	60	65	65	65	65	65	50	65	50	60
3	60	55	55	60	60	60	60	60	45	60	45	55
4	55	50	50	55	55	55	55	55	40	55	40	50
5	50	45	45	50	50	50	50	50	35	50	35	45

Above we set out our assumptions of the average price reimbursed per molecule in each province. We have incorporated a five-quarter market uptake period for each drug, with the average reimbursement ratio in Quarter 5 extrapolated until the end of the CETA delay period. Quarter 5 prices are also used in the allocation of savings by province in Section 4 of the paper.

The assumptions in the average reimbursed price ratio in Alberta, BC, Ontario, and Quebec are based on the publicly stated pricing strategies of the provinces, as of 2012 when CETA could be implemented. We have assumed that average prices following generic entry will be slightly higher than the target prices for two reasons. First, some generic products are sold at prices higher than the targets, because, for example, of high manufacturing, raw material and active pharmaceutical ingredient costs. Second, some sales of a given molecule are expected to be of the branded product at the original price. The declining average price following generic entry is explained by both of these factors The cost of the proposals is made up by difference between the branded and generic versions of the molecules being sold.

Appendix V: Time to Appeal in Cases Commenced Since 2005

PRODUCT	TRIAL JUDGMENT	APPEAL JUDGMENT	TIME IN BETWEEN	TRIAL COURT FILE	APPEAL COURT FILE
Ramipril	26/09/2006	23/04/2007	209	T-1965-05	A-413-06
Celecoxib	01/24/2007	04/30/2007	96	T-1067-05	A-66-07
Lansoprazole	21/11/2006	28/06/2007	219	T-214-05	A-580-06
Venlafaxine Hydrochloride	29/03/2007	01/08/2007	125	T-243-06	A-194-07
Olanzapine	05/06/2007	06/11/2007	154	T-1532-05	A-274-07
Olanzapine	27/04/2007	04/02/2008	283	T-787-05, T-156-05	A-261-07
Clarithromycin BID	26/07/2007	18/03/2008	236	T-1672-06	A-143-08
Atorvastatin	25/01/2007	20/03/2008	420	T-507-05	A-79-07
Sildenafil citrate 25, 50 100 mg tablets	27/09/2007	16/01/2009	477	T-1314-05	A-484-07
Clarithromycin XL 500 mg tablets	08/08/2008	20/03/2009	224	T-135-07	A-622-08
Raloxifene	05/02/2008	27/03/2009	416	T-1364-05	A-84-08
Levofloxacin	17/06/2008	22/06/2009	370	T-1508-05	A-258-10
Ramipril	20/06/2008	08/06/2010	718	T-2300-06	A-379-09
Clarithromycin XL 500 mg tablets	19/06/2009	22/06/2010	368	T-1129-07	A-369-09
Sildenafil citrate 25, 50 and 100 mg tablets	18/06/2009	24/09/2010	463	T-1566-07	A-292-09
Escitalopram (oxalate), 5, 10, 15 and 20 mg tablets	12/02/2009	25/11/2010	651	T-372-07	A-135-09
Escitalopram (oxalate), 5, 10, 15 and 20 mg tablets	12/02/2009	25/11/2010	651	T-991-07	A-129-09
Escitalopram (oxalate), 5, 10, 15 and 20 mg tablets	12/02/2009	25/11/2010	651	T-1395-07	A-139-09
Average number of days delayed by appeal			**374**		