

Drug Market Exclusivity in the EU and Canada: Problems with Norton Rose's Comparative Analysis

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Introduction & Overview

Canada is currently negotiating with the European Union (EU) over the terms of a Comprehensive Economic and Trade Agreement (CETA). As part of these negotiations, the EU has requested that Canada expand intellectual property (IP) rights for pharmaceuticals. This paper is a commentary on a recent report by Patrick Kierans, Kristin Wall and Jill Daley, Canadian IP lawyers with Norton Rose, who have advocated that Canada should agree to the EU's IP demands.

In their recent report, which we term the Norton Rose report,² the authors focus on two differences between the IP regimes in the EU and Canada – patent term restoration and data exclusivity. Both of these affect the period of market exclusivity afforded to new brand (i.e. innovative) drugs. During the exclusivity period, the brand company has a monopoly on the sale of the product. The Norton Rose report concludes that (1) patent term restoration is necessary to compensate for slow Canadian regulatory approval times, and (2) extending data protection in Canada by two years would not extend the total duration of market exclusivity granted to Canadian innovative drugs in most cases.

In this commentary, we demonstrate that these claims contain material inaccuracies that completely undermine the authors' conclusions, as follows:

1. **The Norton Rose Report Uses the Wrong Approval Data:** Due to several methodological and data errors, the Norton Rose report concludes incorrectly that Canada's system is slower to approve new drugs. After correcting these errors, the exact opposite of Norton Rose's conclusion is reached: Canada approved the 22 drugs analysed in Norton Rose report *faster* than the EU.
2. **Extended Data Protection Will Significantly Extend Market Exclusivity for Many Drugs:** The Norton Rose report underestimates the effect of extending data protection on exclusivity periods by omitting key information. The authors excluded drugs having no patent protection or weak patent protection from their sample, *but these drugs are most likely* to have prolonged market exclusivity if data protection is extended. If these weaknesses in patent protection are factored into Norton Rose's analysis, the percentage of drugs having extended market exclusivity jumps from 24% to at least 45%, and likely higher.

The Norton Rose report claim that stronger IP has no material effect on drug spending is suspect. If increasing the minimum term of market exclusivity by two years has no effect on actual market exclusivity, then it should carry no value to brand drug companies. The brand drug industry's strong support for the policy change indicates that it would in fact lengthen actual market exclusivity and hence brand drug revenues. As demonstrated in

¹ This response has been commissioned by the Canadian Generic Pharmaceutical Association (CGPA), although the views expressed in this document are our own. The authors wish to thank Gilbert's LLP for providing invaluable background information on the legal regulation of the pharmaceutical industry.

² Kierans P, Wall K, Daley J (2011) CETA trade negotiations 2011 – drug market exclusivity in the EU and Canada. October 2011. [The Norton Rose report.]

our recent economic impact assessment of the EU's CETA IP demands,³ this lengthened market exclusivity will result in increased costs for Canadians.

Below we set out the background to the Norton Rose report, and our chief concerns about the data and assumptions in the report.

Background to the Norton Rose Report

The Norton Rose report focuses on two suggested reforms proposed in CETA: 1) implementation of patent term restoration (also called “patent term extension”); and 2) an extension of the term of data protection from eight years to 10 years.

Patents have a 20-year term from their filing date in the EU and in Canada. As set out in the Norton Rose report, *patent term extensions* as proposed by the EU in CETA are meant to provide up to 5.5 years of additional exclusivity for drug products if 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 authorization by Health Canada.

Data protection in Canada presently affords eligible innovative drugs with eight years of drug market exclusivity, with the possibility of a six-month extension for submitting pediatric trial data. Generic manufacturers are prevented from filing a comparative drug submission with Health Canada during the first six years of the eight-year term. A generic applicant will not be granted marketing approval until the full eight-year term has expired. The EU is now proposing that Canada increase the period of data protection in Canada from eight years to 10.

Critical Problems with the Analysis in the Norton Rose Report

We identified several critical errors in the Norton Rose report analysis which undermine its two main conclusions. We identify each of these errors below.

1. New Drugs are Approved in Canada Faster than Represented in the Norton Rose Report

a. The Norton Rose Report's Analysis of Drug Approval Timelines

To perform their analysis, Norton Rose selected 22 innovative drugs that have been approved in both Canada and the EU. They then attempted to assemble data on the time taken by the respective regulatory authorities to approve these drugs. All of the drugs selected by the authors were required to have (1) data protection, (2) patents listed on the Canadian Patent Register and (3) a central European market authorization. The authors state they selected the most recently approved drugs but also drugs with “significant IMS global sales”. However, we note that the drugs actually selected by the Norton Rose report are not in fact the most recently approved drugs. Accordingly, the

³ Grootendorst P, Hollis A (2011) The Canada-European Union comprehensive economic & trade agreement. An economic impact assessment of proposed pharmaceutical intellectual property provisions. February 7, 2011.

sample chosen were not chosen by the stated method and are arguably not a “representative” sample.⁴

The authors of the Norton Rose report claim that they “were not able to compare the relative speed of approval [following submission] for the sample drugs selected” because submission dates are not generally available in the public domain. Therefore, they simply compare the dates of approval, and show that for most of the drugs, the approval date was earlier in the EU. Within the group of drugs that they had chosen, the EU approval was on average 451 days earlier. This gives at least the appearance that the regulatory process in Canada is much slower than the EU’s. From this finding, the Norton Rose report concludes that slower approval times in Canada reduce exclusivity periods. The authors of the Norton Rose report then argue that implementing patent term extensions in Canada would compensate (in part) for the patent term benefit lost due to Canada’s slower rate of drug approvals.

b. Faster Approval in Canada than Suggested in the Norton Rose Report

There are several defects in the Norton Rose analysis. First, contrary to the Norton Rose report’s suggestion, data on times from submission to approval are in fact publically available for both the European Medicines Agency (EMA)⁵ and Health Canada.⁶ Strikingly, across the 22 products selected by the Norton Rose report, the submission to Health Canada was on average made 344 days later than the submission to EMA. Second, the time to approval in Canada was only longer because, for four products, the submissions were deemed non-compliant or deficient and more information was requested by Health Canada from the drug companies. These companies then took a long time to file a revised submission. If one excludes the four products, the average time from submission to approval was in fact 67 days quicker in Canada.

Even if one includes all 22 products, but deducts the delay in approval caused by the deficiency of the first submission, the average speed of approval was 50 days quicker in Canada. Actual submission and approval dates for the 22 drugs are shown below.

Drug	Health Canada		European Medicines Agency	
	Submission Filed	NOC Issued	Application Received	Marketing Authorisation Granted
Champix	03/02/2006	24/01/2007	03/11/2005	26/09/2006
Abilify	22/02/2008	09/07/2009	05/12/2001	04/06/2004
Cymbalta**	15/01/2002	01/11/2007	10/10/2003	17/12/2004
Gardasil	12/12/2005	10/07/2006	05/12/2005	20/09/2006
Yondelis	01/06/2009	13/05/2010	27/07/2006	17/09/2007

⁴ The selection description provided by the Norton Rose report suggests that the authors had chosen the drugs with the most recent approval dates. It is easy to verify, however, that the selection is not based on the date of approval. Indeed, five of the selected drugs have approval dates in 2006 and 2007, including the product with the earliest approval date of all 105 drugs in the Registry.

⁵ Data available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/includes/medicines/medicines_landing_page.jsp&mid=

⁶ Data available at <http://www.hc-sc.gc.ca/dhp-mps/prodpharma/sbd-smd/drug-med/index-eng.php#a>.

Drug	Health Canada		European Medicines Agency	
	Submission Filed	NOC Issued	Application Received	Marketing Authorisation Granted
Actemra/Ro-Actemra**	09/04/2008	30/04/2010	29/11/2007	16/01/2009
Brilinta/Brilique	N/A	30/05/2011	27/10/2009	03/12/2010
Ilaris	13/05/2009	26/02/2010	04/12/2008	23/10/2009
Prolia	14/01/2009	06/08/2010	09/01/2009	26/05/2010
Victoza**	02/07/2008	21/05/2010	23/05/2008	30/06/2009
Votrient	16/06/2009	27/05/2010	27/02/2009	14/06/2010
Daxas	10/08/2009	23/11/2010	06/05/2009	05/07/2010
Kuvan	30/07/2009	30/04/2010	30/10/2007	02/12/2008
Jevtana	02/07/2010	16/06/2011	20/04/2010	17/03/2011
Byetta**	30/03/2006	13/01/2011	02/11/2005	20/11/2006
Uloric/Adenuric	31/08/2009	22/09/2010	23/08/2006	21/04/2008
Gilenya	22/03/2010	09/03/2011	22/12/2009	17/03/2011
Cimzia	12/03/2008	12/08/2009	06/06/2008	01/10/2009
Banzel/Inovelon	06/07/2010	22/06/2011	29/03/2005	16/01/2007
Rapaflo/Silodyx/Urorex	21/12/2009	11/01/2011	24/07/2009	29/01/2010
Orencia	06/05/2005	29/06/2006	02/12/2005	21/05/2007
Sprycel	29/03/2006	26/03/2007	12/01/2006	20/11/2006

**Products for which the Canadian submissions were deemed non-compliant or deficient.

Had the Norton Rose report used the correct data, their analysis should have resulted in the conclusion that drugs are approved more quickly in Canada than in the EU.

c. Wrong Data Used to Compare Canadian and EU Approval Timelines

Because the Norton Rose report chose not to analyze the actual time from submission to approval for the 22 drugs, they compared average approval times for all drugs as published by Health Canada and the EMA. They cite Health Canada data showing that the median approval time for 2010 for all “New Drug Submissions” was 433 days. They then examine the EMA 2010 annual report, and claim that it shows an average approval time of 281 days, or “152 days faster than Canada.”

There are two key problems with the EMA data selected by the Norton Rose report. First, while *assessment* averages 281 days in Europe, the EMA report clearly states that *approval takes an additional 79 days beyond the assessment period.*⁷ **The Norton Rose report thus simply used the wrong data.** Compounding this error, almost half of the EMA approvals were for “generic or hybrid medicines and informed consent applications” which are obviously very different in nature from the New Drug Submissions in the Canadian data. The authors of the Norton Rose report therefore compare the approval times of new brand drugs in Canada with an average “assessment” time of new brand and generic drugs in the EU, an obviously invalid comparison.

⁷ European Medicines Agency 2010 Annual Report, p 25, Fig 19. June 28, 2011.

2. Extending Data Protection Will Extend Drug Exclusivity Periods for Many (If Not Most) Drugs

a. Norton Rose's Analysis of Extending Data Protection in Canada

The Norton Rose report finds that of the 22 drugs they selected, only eight of the drugs had total market exclusivity terms that would be extended, if Canada were to adopt the EU's data protection regime. The remaining drugs are said to have patent protection that extended beyond the term of data protection, meaning that the extension of data protection from eight to 10 years would have no impact in the case of 14 of the 22 drugs examined.

The Norton Rose report also examines a larger group of drugs – all 105 drugs listed on Health Canada's Register of Innovative Drugs. Of these drugs, 81 had patents listed on the Patent Register and 58 out of the 81 (72%) benefited from patent terms that extended beyond the data protection term. Based on these results, the Norton Rose report concludes that because the total market exclusivity period is generally governed by patent terms, and not by the term of data protection, the extension of data protection from eight years to 10 will provide certainty to brand name companies without extending the market exclusivity period in most cases.

b. No Basis for Removing Unpatented Drugs from the Analysis

The Norton Rose report's conclusion on data protection is based on the assumption that additional data protection would not affect exclusivity periods because patent terms are longer still. Even if we accept this assumption, which we do not (see next subsection), their conclusion is flawed due to a major omission in their analysis.

The authors state that 81 of 105 of the drugs have listed patents. **They then arbitrarily exclude the remaining 24 drugs without listed patents from their analysis.** However, there is no principled basis for excluding this set of drugs, which may still be protected by unlisted patents. Regardless, given the lack of listed patents, **the authors of the Norton Rose report must have understood that these 24 drugs would be most affected by a two-year increase in data protection precisely because they have no listed patents.**

As a result, the Norton Rose report minimizes the impact of extending data protection. To be complete, the 24 drugs without listed patents should have been included in the calculation and thus all 105 drugs should have been included in the denominator. To now restate their conclusion more accurately, *at most 58 out of 105 (55%) - not 72% - of the drugs would have benefited from patent terms that extended beyond the data protection term. The remaining 45% of drugs (47 out of 105) would enjoy an automatic two-year increase in total market exclusivity periods if data protection were extended.*

c. The Norton Rose Report Improperly Assumes that All Listed Patents are Valid

The Norton Rose report assumes that if a patent term extends beyond the data protection term, there is no impact on total market exclusivity by a CETA extension because patent protection opaquely masks data protection.

However, this reasoning is flawed because patent protection is not absolute – in some cases, generic drugs do not infringe patents, and in other cases patents are judged to be invalid before they expire. Drug patents cover different types of subject matter, such as molecules, uses, formulations and processes. Some types of patents are inherently stronger than others. For example, new molecule patents (if properly drafted and based on proper supporting data) are rarely judged to be invalid, while patents to slight optimizations of a formulation are more often found invalid.

When pharmaceutical patents are litigated in Canada, many are not upheld by Canadian courts. In fact, *approximately two-thirds of litigated pharmaceutical patents are found to be invalid or not infringed.*⁸ When generic companies successfully invest in litigating these patents, they open the market to generic entry earlier than would otherwise occur, leading to consumer savings. There are currently drugs with patents listed on the Patent Register expiring several years from now (such as Lipitor with patent expiry dates as late as 2022), but the patents actually blocking generic entry were found invalid by the courts, resulted in generic competition *12 years before* the expiry of the last patent.

Therefore, simply because a patent lasts an extra 4.5 years beyond data protection (as stated in the Norton Rose report) does not necessarily mean that the patent life governs the total market exclusivity period. There is a reasonable expectation that if challenged, many of those patents will be found invalid. An extension of data protection would therefore extend the total market exclusivity period not only for drugs not having overlapping patent protection but also for drugs poised to lose patent protection following a successful patent challenge. Extending data protection would delay the time until a generic company could even begin to challenge weak patents.

Conclusions

This report has shown that the conclusions in the Norton Rose report are compromised due to errors and omissions in the data used. In particular, the Norton Rose report suggests that “Canadian innovators” are “doubly disadvantaged” compared with those in the EU. This is simply not the case:

- First, innovative drug approvals are *not* in fact slower in Canada, negating the Norton Rose report’s justification for longer market exclusivity periods.
- Second, the Norton Rose analysis completely ignores drugs that do not have patents, or drugs having patents that may be found invalid, and it is these drugs that are most impacted by increased data protection.
- Third, the Norton Rose report does not consider the IP protections available in Canada but unavailable in the EU, such as patent linkage and the absence of an administrative patent opposition process.

Finally, in reviewing the Norton Rose report, we were struck by the authors’ conclusion that the changes in IP rights for pharmaceuticals, for the majority of sampled products, will “provide greater security for innovators without extending overall IP exclusivity for innovative medicines.” It is evident that if a given measure increases “security” in this

⁸ Health Canada Notice, “Release of the Therapeutic Products Directorate Statistical Report 2010 for the *Patented Medicines (Notice of Compliance) Regulations* and Data Protection”. July 28, 2011.

sense, it must have the effect of extending the exclusivity period. Otherwise the measure is doing nothing at all. It is correct, of course, that the increase in exclusivity period for different drugs will vary, depending on a variety of factors. It is, however, misleading to claim that there is an increase in “security” but no increase in the exclusivity period.

The implications of extending pharmaceutical IP protection in Canada are significant – such extensions will inevitably result in the slower arrival of competition in drug markets. Those who advocate that Canada acquiesce to the EU pharmaceutical IP demands cannot justify their position by claiming that Canadian approval times are particularly slow or that the IP demands will have no effect on market exclusivity periods. Both of these claims are false.