

Recent Changes in the Law Affecting Generic Drug Market Entry, and the Impact for Drug Prices

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Introduction

It is obvious that generic drugs cost less than drugs sold under a drug monopoly. In 2005, the average cost of brand-name prescriptions was \$63.79, while the average cost of a generic prescription was \$25.02.

Therefore, perhaps the most important factor affecting overall drug prices in Canada is: how soon can a generic version of any given drug enter the market?

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This is almost entirely a matter of federal law. There have been some changes to these laws in recent months.² This paper will attempt to provide an overview of the changes, some of which are regulatory, and some of which result from court decisions, in particular a decision of the Supreme Court of Canada, *Apotex v. AstraZeneca*, 2006 SCC 49 (“*AstraZeneca*”).

The important question to consider while reviewing the changes, I think, is: what effect will there be on the actual availability of generic products in the market?

As we will see, this is not an easy question to answer. For each of the recent regulatory changes that might conceivably speed up the market entry of generic drugs, the transitional provisions or some other factor reduce the impact in the real world. Other regulatory changes, in particular the 8 years of “data protection” will clearly slow down the market entry of generic drugs.

The federal government in fact seems to have intended that the regulatory changes not have much impact. The Regulatory Impact Analysis Statement (“RIAS”), the explanatory text that accompanies the recent regulatory changes, speaks of the need for “balance”, which may be another way of saying “our goal is to make the rules more complicated, without actually changing their effect at the end of the day.”

² There have also of course been important amendments affecting the provincial reimbursement scheme in Ontario, and similar changes are likely in other provinces. But those changes are being covered by other speakers.

On balance I would say that the net effect of the regulatory changes is probably to slow down the introduction of generic drugs. The recent Supreme Court of Canada decision however may have some effect in the opposite direction. Time will tell.

Rate of generic substitution

Canada is diverging from the U.S. in terms of the percentage of all prescriptions filled by generics in the market place. In both countries, generic substitution has increased due to some major patent expiries, but the rate of increase has been much slower in Canada.

Ten years ago, the percentage was about the same: about 41% of prescriptions were filled with generic drugs in Canada versus about 40% in the US.³ By 2006, there had been an increase in the prescriptions filled by generics in Canada to 46%,⁴ but a much more rapid increase to about 63% of prescriptions filled by generics in the U.S.⁵

This difference, I think, shows it is now much more difficult to get a generic drug on the market in Canada than in the US, largely because of evergreening strategies and the delays created by the poorly drafted NOC Regulations. Omeprazole, for example, to cite one well known drug, was genericized in the US years before it was in Canada.

³ “Policy Relating to Generic Medicines in the OECD”, National Economic Research Associates, Economic Consultants, a table prepared for the European Commission, Table 4.2., p. 24, cited in Hore, E. “A Comparison of United States and Canadian Laws as they Affect Generic Pharmaceutical Market Entry,” Food and Drug Law Journal, Vol 55, Number 3, 2000, p. 373, note 4.

⁴ IMS data.

⁵ Generic Pharmaceutical Association.

The numbers involved are huge, as everyone at this conference knows. In 2006, expenditure on prescription drugs reached \$21.1 billion nationally in Canada, and \$8.5 billion in Ontario alone.⁶

An important difference between the US and Canada, however, is that drug prices are a hot political issue in the US, but not here. This is because many seniors and other people in the US pay directly for drugs. In response to political pressure from seniors, George Bush himself introduced laws intended to limit “evergreening” of pharmaceutical patents with a speech at the White House in 2002.⁷

In Canada, by contrast, drug prices, and the availability of generic drugs, do not have the same political immediacy. Seniors in Canada are covered by the provincial drug plans. Almost everyone is insulated from the cost of drugs somehow, either through a public or private plan. Of course, we all pay in the end, either through taxes or in some other way. But the fact remains that drug prices in Canada are an abstraction of interest mainly to government and benefit industry technocrats dealing with arcane matters such as demographic projections, budgets, government deficits and so on.

⁶ Canadian Institute for Health Information “Drug Expenditure in Canada 1985-2006” released May 15, 2007. The figure reported for prescription drug expenditure in Canada is followed by the following footnote: “Since the NHEX [National Health Expenditure database] consists of macro-level health expenditure data, some over-the-counter drugs and personal health supplies that are covered under some drug benefit plans may be counted as prescribed drug expenditure.”

⁷ Remarks by the President on Prescription Drugs, The Rose Garden, October 21, 2002. See <http://www.whitehouse.gov/news/releases/2002/10/20021021-2.html>

Therefore, the large 18% discrepancy in generic drug substitution between the US and Canada has gone largely unnoticed.

At the end of the day, policy makers, I would suggest, have to decide what the rate of generic substitution in Canada should be, compared with other jurisdictions. The laws discussed in this paper are mechanisms to prevent market entry by generic products. They do not apply to other industries. They go well beyond Canada's treaty obligations. They are in effect an indirect subsidy from taxpayers and benefit payers to a favoured industry segment.

It will be interesting to see whether these laws prove to be sustainable in the long run, as the Canadian population ages, and drug budgets are put under serious strain.

Summary of amendments

The recent changes fall roughly into three groups:

1. **Amendments to the *Patented Medicines (Notice of Compliance) Regulations* (“NOC Regulations”)**: These were passed on October 5, 2006. Some of the changes are good for generics, and some bad.
2. **The *AstraZeneca* case**: This case has had much more immediate effect than the regulatory amendments to the NOC Regulations so far. Assessing its full effect at

this point is premature because much depends on how it is interpreted by the lower courts.

3. **“Data Protection” amendments to the Food and Drug Regulations:** At the same time it amended the NOC Regulations, the government amended the *Food and Drug Regulations*, to impose an eight year ban preventing the grant of regulatory approval to generic manufacturers, regardless of the presence or absence of patents. This far reaching regulation purports to create a whole new category of intellectual property.

Amendments to NOC Regulations

The changes passed on October 5, 2006, are designed, at least in part, to prevent “evergreening”. Evergreening, in brief, means the use of marginal patents to repeatedly trigger the automatic 24 month stay under the NOC Regulations, thus extending the patentee’s monopoly.

Under the amendments, generic manufacturers need only address patents listed before the generic submission is filed. That means only patents listed before the generic submission is filed can be used to trigger the 24 month automatic stay. Formerly, any listed patent had to be addressed, even if listed on the register 24 hours before the NOC was to be granted.

As well, the amendments put limits on the types of patents that can be listed with the initial innovator new drug submission (NDS) to Health Canada, or with supplements to a new drug submission (SNDS). Transition provisions ensure these changes may not have much immediate impact.

There were also what may be significant changes in the damages provision under the NOC Regulations.

In order to explain what all this means, it is necessary to go back and explain briefly how the NOC Regulations work, and also the “evergreening” problem that the amendments are intended to fix.

How the NOC Regulations work

The NOC Regulations, originally passed in 1993, have been described as a “draconian regime” by the Supreme Court of Canada.⁸ In effect, they allow a pharmaceutical drug company with rights to a patent, called a “first person” in the arcane language of the NOC Regulations, to keep a competing generic product off the market for 24 months merely by *asserting* that its patents may be infringed. No such automatic relief is available to patentees in other industries.

As Justice Frank Iacobucci of the Supreme Court of Canada put it:

⁸ *Merck Frosst v. Canada (Minister of National Health and Welfare)* (1998), 80 C.P.R. (3d) 368 (S.C.C.) at 384 (“*Merck Frosst*”).

The Regulations provide for what is, in effect, a statutory prohibition on, or injunction against, the granting of a NOC, commencing immediately upon the filing by a "first person" of an application for a court-imposed prohibition order and concluding only upon the earlier of the judicial determination of the application or the passage of 30 months. This prohibition takes effect automatically, without any consideration of the merits of the application; not even the ordinary requirements for an interlocutory injunction must be complied with.⁹

In brief, the procedure under the NOC Regulations is as follows:

The register: Patentees, referred to as "first persons," may list patents on a patent register in connection with drug products for which they hold regulatory approval.

Health Canada maintains the register.

Allegation: If a generic manufacturer, referred to as a "second person," files a submission for regulatory approval to sell a drug in Canada that makes a comparison or reference to the first person's drug, i.e. is an Abbreviated New Drug Submission (ANDS), the Minister of Health, the federal health and safety regulator, may not grant regulatory approval (a notice of compliance or NOC) to the generic drug until the conclusion of non-binding preliminary litigation as to whether the first person's patents are valid and infringed. That is, health and safety approval of the generic drug is made contingent not only on the drug being found to be safe and effective by the regulator, but is also tied to a preliminary assessment of patent issues by the courts.

⁹ *Merck Frosst, supra.*

When it files its submission, the generic manufacturer or “second person” must either accept that it will not get regulatory approval until expiry of all listed patents, or serve a “notice of allegation” (NOA) on the first person, in which it asserts that the listed patent or patents are invalid or are not infringed by its proposed generic version of the drug, together with a detailed statement of the legal and factual basis of the allegation.

Judicial review application: The first person, on being served with an NOA, may within 45 days commence a judicial review application in the Federal Court for an order that the NOC not be issued for the generic drug until expiry of its patent or patents.

Automatic stay: If such an application is commenced, the Minister may not issue an NOC for 24 months, or until the court hearing or patent expiry. As the Federal Court of Appeal stated, “By merely commencing the proceeding, the applicant obtains what is tantamount to an interlocutory injunction for up to 30 months [as the time frame then was] without having satisfied any of the criteria a court would require before enjoining issuance of an NOC.”¹⁰

Prohibition order: At the hearing of a judicial review application under the NOC Regulations the court must decide whether the generic manufacturer’s allegation of non-infringement or invalidity is “justified.” If the first person establishes the allegation is not justified, the court must issue an “order of prohibition,” preventing the Minister from

¹⁰ *Bayer A.G. v. Canada (Minister of National Health and Welfare)* (1993), 163 N.R. 183 at 189-90, 51 C.P.R. (3d) 129 (F.C.A.).

issuing the NOC to the generic manufacturer until patent expiry. If the court finds the allegation is justified, the application is dismissed, and an NOC may be granted once Health Canada's regulatory review is complete (assuming no other prohibition applications are commenced in respect of the same generic drug submission).

Nature of the litigation: The litigation started by the first person after receiving an NOA is not an action for patent infringement, but a judicial review application. In theory the litigation is "summary" i.e. quick. In practice, such court cases have become more and more complex, usually involving extensive expert evidence. A convoluted body of procedural jurisprudence has grown up unique to these kinds of cases. There are many procedural pitfalls and peculiarities. For example, the generic is not allowed to amend its notice of allegation, but must nevertheless raise every legal and factual issue in its NOA it will rely on at the hearing two years away. The generic manufacturer thus must advance every legal and factual issue it may conceivably ever wish to raise, and anticipate and respond in advance to every argument the first person may make, before it knows what those arguments are. Since every argument and fact must be in the NOA, and the case is lost if the NOA is deemed to be "deficient" at the hearing, NOAs have been getting steadily longer and more complex. It is not uncommon for a NOA to be over a hundred pages long. Thus rules designed to make the proceeding "summary" have had the perverse result of making it more complicated.

Procedurally, the litigation consists of an exchange of affidavit evidence and cross-examination, followed usually by a hearing that may be from one to five days or more. Although such judicial review proceedings are theoretically “summary” in nature, they may take years to get to a hearing.

Patent issue is not determined: The issue of patent infringement or validity cannot be determined in NOC proceedings; “their object is solely to prohibit the issuance of a notice of compliance under the *Food and Drug Regulations*.”¹¹ The remedies under the NOC Regulations are in addition to the remedies available to any patentee under the *Patent Act*.

The odd result is that a second person might lose the prohibition proceedings under the NOC Regulations, i.e. be unable to enter the market due to a prohibition order, yet later establish at a full trial under the *Patent Act* that the patent is both invalid and not infringed.¹² Conversely, the second person might win the prohibition application, but later lose under the *Patent Act* at a trial involving the same drug and the same patent.¹³

¹¹ *Merck Frosst v. Minister of National Health & Welfare* (1994), 55 C.P.R. (3d) 302 at 319 (F.C.A.).

¹² See for example *Apotex Inc. v. Syntex Pharmaceuticals International Ltd.* (1999), 1 C.P.R. (4th) 22, 166 F.T.R. 161 (F.C.T.D.).

¹³ This occurred for example with levofloxacin. See *Janssen-Ortho v. Novopharm*, 2004 FC 1631, appeal dismissed as moot, January 6, 2005, in which prohibition proceedings were dismissed because the allegation the 080 patent was invalid was justified, however, the same patent was found valid and infringed at a trial in *Janssen-Ortho v. Novopharm*, 2006 FC 1234, appeal A-500-06 now under reserve.

Thus the NOC Regulations create a kind of double jeopardy. They involve the parties and the courts in litigation which, despite its high cost and complexity, does not resolve the real issue between the parties: is the patent valid and infringed or not?

The generic manufacturer has no option but to fight and win years of litigation under the NOC Regulations before it can get its product on the market and earn revenues. Yet after it wins the litigation, the generic manufacturer can then be sued again under the *Patent Act* on the same drug and the same patent.

Link with “early working”: Authority to pass the NOC Regulations is created by section s. 55.2(1) and (4) of the *Patent Act*, which limit the purpose of the regulations to preventing abuse of the “early working” exception. The “early working” exception in s. 55.2(1) creates an exception from patent infringement covering a person who uses or works a patented invention for purposes reasonably related to the submission of regulatory information.

In *Bristol-Myers Squibb Co. v. Canada (Attorney General)*¹⁴ (“*Biolyse*”), the Supreme Court of Canada stated that the NOC Regulations must be interpreted in light of this limited purpose. If the generic manufacturer does not or cannot “early work” the patent,

¹⁴ 2005 SCC 26. At issue was Biolyse’s New Drug Submission (NDS) for a drug containing paclitaxel obtained from a different source than the BSM product TAXOL. Biolyse submitted clinical trials to the regulator in its NDS, rather than a bioequivalence comparison study with TAXOL.

the NOC regulations do not apply to that patent. This limited purpose of the NOC Regulations is also the basis of the recent *AstraZeneca* case, as we will see.

Damages: Section 8 of the NOC Regulations allows for the generic manufacturer to seek damages, if wrongly kept off the market. There are many cases now before the courts in which damages are sought, but they are still on-going. There has been no award of damages in any of these cases yet.

What is evergreening?

As mentioned above, the recent amendments attempt to curtail “evergreening,” a term sometimes used to describe various strategies involving the use of the automatic stay in the NOC Regulations to prevent competition after basic patent protection on a drug product has expired.

It will be recalled that under the procedure in the NOC Regulations:

- A 24-month stay on approval of a generic drug occurs automatically if a “first person,” a brand-name drug company, commences an application for a prohibition order.
- Under the old regulations (i.e. as they read prior to October 5, 2006), even if a second person has already filed its ANDS, and even if it is already subject to the 24-month stay, it still must address any newly listed patents that may appear on

the register at any time before it gets an NOC, thus re-triggering a further 24 month stay.

Under the old regulations, this process could be repeated indefinitely, allowing a patentee to use weak patents claiming coatings, crystalline forms, manufacturing processes, new uses etc. to trigger new stays and prevent competition.

The resulting delay in the market entry of a generic drug under the old regulations was often lengthy, as can be shown from the following chronology in respect of paroxetine, an anti-depressant:

- Apotex filed an abbreviated submission for Apo-paroxetine on August 29, 1997, and served NOAs to the four patents listed on the patent register at the time.
- SmithKline Beecham commenced two applications in response to the allegations (T-2660-96 and T-2230-97), triggering the stay.
- While those cases were before the court, SmithKline listed a further patent (the '637 patent), on February 17, 1998.
- SmithKline's two earlier applications were dismissed April 20, 1999¹⁵ i.e. the court found Apotex's allegations of invalidity and non-infringement were justified, but Apotex was unable to obtain its NOC because the '637 patent had meanwhile been listed.
- Apotex's submission entered "patent hold" status on October 9, 1999 (i.e. TPD's health and safety approval process was complete).

¹⁵ *SmithKline Beecham v. Apotex* (1999) 1 C.P.R. (4th) 99, affirmed (2001) 10 C.P.R. (4th) 338 (F.C.A).

- Apotex served an allegation that the '637 patent was invalid. SmithKline commenced a new application (T-677-99), re-triggering the stay. This application was dismissed on July 6, 2001;¹⁶ the Court found Apotex's allegation of invalidity was justified.
- While the litigation on the '637 patent was pending, SmithKline added more patents to the register.
- Apotex served an allegation to the '575 patent, resulting in a new prohibition application (T-1059-01), triggering a further automatic stay. That case was dismissed on May 30, 2003; the court found Apotex's allegation of double patenting to be justified.¹⁷
- However, another prohibition proceeding had meanwhile been commenced against Apotex concerning 3 further patents on "Form A" (T-876-02).¹⁸
- Several generic parties finally received NOCs in October 2003, when Genpharm, another generic company, also won prohibition proceedings on some of the same patents already litigated by Apotex,¹⁹ and SmithKline (now owned by GSK) seems to have decided that the risk of damages outweighed the benefit of continuing to litigate.

As a result of all this, the delay in market entry of the generic product was about four years after the health and safety approval process was complete, yet the generic

¹⁶ *SmithKline Beecham v. Apotex* (2001) 14 C.P.R. (4th) 76, affirmed (2002) 21 C.P.R. (4th) 129 (F.C.A.)

¹⁷ *GlaxoSmithKline v. Apotex* 2003 FCT 687.

¹⁸ A motion to get this case dismissed on the grounds the patents were not eligible for listing was dismissed *GlaxoSmithKline v. Apotex* 2003 FC 1055.

¹⁹ *GlaxoSmithKline v. Genpharm* 2003 FC 1248.

manufacturers' NOAs were found to be justified in every case that went to a hearing. That is, Apotex's generic product did not infringe valid patents.²⁰ In the third case mentioned above, T-1059-01, the court commented on the patentee's multiple patent strategy as follows:

The effect of [the 24 month automatic stay] is to put in place a mandatory injunction that remains in force until either the case is disposed of or the 24-month stay expires. The addition of additional patents allows the patent-holder to bring additional applications, thereby obtaining multiple injunctive periods. There is no need to look further than the case at bar for an excellent example of this practice. Even though Apotex successfully invalidated the '637 patent in 2001, the filing of this application by GSK has prohibited Apotex from bringing its product to market for the past two years.²¹

Approximately 75% of the prohibition applications under the NOC Regulations decided by a court since 1998 have been dismissed. That is, the generic "second person" wins most of the time. But, as the above example shows, even when a generic manufacturer "wins" several prohibition applications with respect to a particular drug, there may be further automatic stays that keep its product off the market.

As the Regulatory Analysis Impact Statement ("RIAS") published with the October 5, 2006 amendments, observes: "an innovator company may delay generic market entry by listing new and sometimes irrelevant patents on the basis of minor product revisions ... such that generic companies may be prevented from entering the market with a competing version of the original innovator product even when the original patents have

²⁰ The findings in these prohibition cases did not finally determine the patent issues, as explained above. However, SmithKline never exercised its right to bring a separate action for infringement.

²¹ 2003 FCT 687, paragraph 88.

long since expired or been addressed.” The brand company can thus obtain “repeat 24-month stays against the same generic competitor.”

The RIAS also mentions “a number of recent court decisions” which “have given rise to the need to clarify the patent listing requirements. These decisions, which relate to timing and relevance issues, are not a function of judicial error but rather of deficiency in the language of the PM(NOC) Regulations themselves.” That is, the government admits that it fouled up in drafting the NOC Regulations.

The “recent decisions” which arose from “deficiency in language” in the old regulations are *Apotex v. Minister of Health*²², which held that a “submission” for the purposes of the time limit on patent listing in s. 4(4) includes a supplement to a new drug submission (“SNDS”), and *Eli Lilly v. Minister of Health*²³, in which the court held that patents on non-approved formulations can be listed on the patent register. In effect, these cases made the timing and subject matter restrictions on listing patents easy to evade. For example there are now, I believe, approximately eighteen patents listed for atorvastatin, eleven for omeprazole magnesium, and nine for clarithromycin.

Generic manufacturers say the NOC Regulations are unnecessary, and should be repealed. They say patentees in the pharmaceutical industry should have the same rights to enforce their patents under the *Patent Act*, as do patentees in any other industry. There should not be additional automatic remedies.

²² *Apotex v. Minister of Health* (1999), 87 C.P.R. (3d) 271, affirmed (2001) 11 C.P.R. (4th) 538.

²³ *Eli Lilly v. Minister of Health*, 2003 FCA 24.

Recent amendments to the NOC Regulations

The government did not to repeal the regulations, as the generic industry wanted, but instead amended the NOC Regulations on October 5, 2006.²⁴ The main purpose of the amendments was to fix the “deficiencies in the language” of the Regulations. The government’s view seems to have been that the problems arose from poor drafting, not from any fundamental flaw in the underlying idea of an automatic stay for pharmaceutical patentees.

The major changes are:

Patent register is “frozen” as of the “date of filing” of the generic submission with Health Canada. This means the generic manufacturer need send an NOA only in respect of patents listed on the register on that day (s. 5(4)). It need not address patents that may be listed later. The old practice was that a generic had to send an NOA in respect of all patents listed at any time before the generic NOC was issued, no matter when the patents were added to the register. However, the transition provision is important: if the generic submission was filed before October 5, 2006, the deemed “date of filing” is October 5, 2006, not when the submission was actually filed. This means the amendments have had little effect in on-going litigation over evergreening patents involving many generic drugs.

²⁴ *Regulations amending the Patented Medicines (Notice of Compliance) Regulations*, SOR/2006-242 published October 18, 2006, Canada Gazette, Part II, pp. 1503 – 1525.

Tightened listing requirements: The previous practice was that there did not need to be any connection between the patent and the SNDS with which it was submitted. As well, patents on non-approved formulations and uses could be listed. Under the amendments, patents can be listed with an NDS for the medicinal ingredient, the formulation, the dosage form, or the use, but the medicinal ingredient, the formulation, the dosage form, or the use must be approved. Patents on a change in formulation, a change in dosage form or a change in use can be listed with an SNDS but must claim the changed formulation, dosage form or use. Again, the transition provision is important: patents submitted prior to June 17, 2006 are unaffected. Some patents listed after that date that do not meet these requirements appear to have been recently de-listed. However, the NOC Regulations were also broadened to allow patents claiming a “dosage form” to be listed.

Changes re damages: The other significant change to the NOC Regulations on October 5, 2006, was that the damages provision, section 8, was amended to modify wording which used to say that a generic manufacturer whose product was wrongly kept off the market under the NOC Regulations could sue for “damages or profits.”²⁵ Henceforth, the generic can only get “damages”. Under the transition provision, this change does not apply to any section 8 case commenced before October 5, 2006.

²⁵ Former subsection 8(4) read: “The court may make such order for relief by way of damages or profits as the circumstances require in respect of any loss referred to in subsection (1).”

It is unclear how significant the change is because the courts have not yet ruled on what the old language meant. In the cases already seeking “damages and profits” under section 8, generic manufacturers argue that the phrase “damages or profits” means that they can be awarded not only lost profits resulting from delays in approval of their drugs, but also to disgorgement of the first person’s profits during its period of unjustified monopoly. “Profits” were included, they argue, to create a disincentive to abuse the NOC Regulations. The innovator companies, on the other hand, argue the words “or profits” meant the *generic manufacturer’s* lost profits i.e. that “damages” and “profits” were synonymous.

Changing the wording has removed a potential downside to the abuse of the NOC Regulations by first persons where on-going evergreening strategies were still on-going as of October 5, 2006, or in future cases. A section 8 case can only be commenced after the NOC is granted to the generic manufacturer.

The AstraZeneca case

Because of the lengthy transition provisions, the regulatory changes have not had much discernible effect so far. What has had a major effect is the Supreme Court of Canada’s decision in *AstraZeneca* released November 3, 2006, after the amendments of October 5, 2006, but without making reference to those amendments.

Applying *Biolysse*, the Court ruled that only patents that the generic manufacturer “early worked” in preparing its submission need to be addressed under the NOC Regulations. This could make evergreening strategies involving late listed patents impossible under the old NOC Regulations, which apply in all the on-going cases. It is not yet clear how the case will affect the interpretation of the amended NOC Regulations.

In *AstraZeneca*, patents were listed for AstraZeneca’s omeprazole capsules years after Apotex submitted its ANDS for a generic equivalent. The Supreme Court held Apotex could not have “early worked” these patents, and therefore did not need to address them by sending an NOA.²⁶ Therefore, the Minister was right to issue an NOC to Apotex for its generic version of omeprazole.

The *AstraZeneca* case potentially affected many other generic drugs also held up by the NOC Regulations. For example, the Minister applied the *AstraZeneca* case to issue generic NOCS to ramipril, in December 2006, and to desmopressin in January, 2007.

The Minister’s interpretation of *AstraZeneca* was that a second person need not address a patent on the register if it acquired the "comparator" drug used in its bioequivalence studies before the brand submission was filed which led to the NOC with which the patents were listed. (Patents are often out of time to be listed against the original brand

²⁶ They were not capable of being early worked by Apotex because Apotex acquired the omeprazole capsules before the patents in question issued.

NDS and are therefore submitted with later SNDSs.) As well, the generic submission must not have "made use of" any changes in NOCs with which the patents were listed.

There was of course litigation over whether this interpretation was correct, and whether the Minister of Health was correct to have issued the ramipril and desmopressin NOCs.²⁷ Justice Hughes for the most part upheld the Minister's interpretation, with minor changes, in the *Ferring* decision.²⁸

About a month later, Justice Hughes also applied *AstraZeneca* in another case, but in a different way. In *Wyeth Canada v. Ratiopharm*,²⁹ concerning venlafaxine, the issue was whether the patent was properly listed with the various SNDSs with which it was purported to have been listed. In that case, Hughes reviewed the *AstraZeneca* decision and interpreted it to mean that, in order for a patent to be properly listed on the register, it must be "relevant" to the NOC which resulted from the first person submission for which it was listed. He found that the patent in question was relevant to some of Wyeth's NOCs, but not others. This case could have a significant impact, because there are many patents listed with SNDSs which do not relate to the subject matter of the SNDS.

Both the *Ferring* and *Wyeth* decisions are under appeal.

²⁷*Ferring et al. v. Minister of Health*, 2007 FC 300. Various appeals are to be heard in September.

²⁸ He proposed that the relevant date should be not when the generic acquires the product but when it files its submission, and that the changes made by the generic must be those as specified in section 5(1) of the NOC Regulations, namely, for the purpose of bioequivalence.

²⁹ 2007 FC 340. An appeal is to be heard June 25, 2007.

Do not worry if you find these rules hard to follow. The Regulations were from the outset designed to be confusing, because, given the automatic regulatory stay, the more confused and irrational the rules, the longer it was likely to take for a generic product to be approved.

“Data Protection” amendments to the *Food and Drug Regulations*

At the same time the NOC Regulation amendments were passed, the government also amended the *Food and Drug Regulations*.³⁰ Sometimes referred to as the “data protection” amendments, the amended regulations grant an eight year period of exclusivity to brand companies to market new drugs free of competition. The period of exclusivity operates independently of any patent.

Under the old regulations, once an NOC issued for an innovative drug, no one else could obtain an NOC in respect of that drug through the abbreviated submission process for a period of five years if the regulator relied on the data in the innovator file at Health Canada to approve the generic submission. Such reliance rarely or never occurred in practice because the regulator did not review the data in the innovator submission when reviewing the generic submission.

The most important changes are in section C.08.004.1 of the *Food and Drug Regulations*, and can be summarized as follows:

³⁰ *Regulations Amending the Food and Drug Regulations*, published October 18, 2006 in the *Canada Gazette Part II*, Vol. 140, No. 21, SOR/DORS/2006-241 at pages 1493-1494.

- **Eight years' data protection for medicinal ingredient, if not previously approved:** The new amendments introduce an eight year ban on generic competition from the date the innovator drug is first approved, if the medicinal ingredient was not previously approved.³¹ The new amendments also introduce a six-year “no-filing” period within the eight-year term,³² that is, the generic manufacturer may not file its regulatory submission during the six-year period.
- **Six month pediatric exclusivity:** If pediatric studies are included in the brand submission and the Minister finds they “were designed and conducted for the purpose of increasing knowledge”, the 8 years of exclusivity becomes eight and a half years.³³

The RIAS states that these amendments were brought in to “clarify and effectively implement Canada’s North American Free Trade Agreement (“NAFTA”) and the Trade Related Aspects of Intellectual Property Rights (“TRIPS”) obligations with respect to data protection.” Those provision require that trade secrets such as confidential data in the brand’s regulatory submission must be protected, and that another party cannot “rely on” such data to get approval for its drug for five years

The relevant wording of NAFTA is in Article 1711: Trade Secrets, subparagraphs 5 and 6:

5. If a Party requires, as a condition for approving the marketing of pharmaceutical or agricultural chemical products that utilize new chemical entities, the submission of undisclosed test or other data necessary to determine whether the use of such products is safe and effective, the **Party shall protect against disclosure of the data** of persons making such submissions, where the origination of such data involves

³¹ C.08.004.1(3)(b), as amended

³² C.08.004.1(3)(a), as amended.

³³ C.08.004.1(4), as amended.

considerable effort, except where the disclosure is necessary to protect the public or unless steps are taken to ensure that the data is protected against unfair commercial use.

6. Each Party shall provide that for data subject to paragraph 5 that are submitted to the Party after the date of entry into force of this Agreement, no person other than the person that submitted them may, without the latter's permission, **rely on such data in support of an application for product approval during a reasonable period of time after their submission.** For this purpose, a reasonable period shall normally mean not less than **five years** from the date on which the Party granted approval to the person that produced the data for approval to market its product, taking account of the nature of the data and the person's efforts and expenditures in producing them. Subject to this provision, there shall be no limitation on any Party to implement abbreviated approval procedures for such products on the basis of bioequivalence and bioavailability studies.

The less specific wording of the TRIPS Agreement is in Article 39, paragraph 3:

3. Members, when requiring, as a condition of approving the marketing of pharmaceutical or of agricultural chemical products which utilize new chemical entities, the submission of undisclosed test or other data, the origination of which involves a considerable effort, **shall protect such data against unfair commercial use.** In addition, Members shall protect such data against disclosure, except where necessary to protect the public, or unless steps are taken to ensure that the data are protected against unfair commercial use.

Canada already had a provision to protect such data in the *Food and Drug Regulations*.

The Federal court of Appeal held in the *Bayer* case in 1999 that that section was in compliance with NAFTA.³⁴ The Court said that approval of a generic product through bioequivalence testing does not affect the brand's right to confidentiality in its data because that data remains confidential. The regulator does not "rely" on the data unless it examines the data in the innovator file while reviewing the generic submission, which it typically does not do.

³⁴ *Bayer v. A.G. Canada* (1999), 87 C.P.R. (3d) 293, leave to appeal to Supreme Court of Canada denied (1999) SCCA No. 386. At the hearing, Bayer also relied on the less stringent requirement in TRIPS Article 39, paragraph 3 but the Court did not refer to TRIPS in its reasons. No complaint about Canada's long-standing interpretation has ever been made under the dispute settlement process in TRIPS or NAFTA.

The Court stated:

Specifically, if a generic manufacturer is able to establish the safety and effectiveness of its product on the basis of bioequivalence or bioavailability studies without the Minister having to examine and rely upon confidential data filed by the innovator, there is no reason or justification for the minimum five year protection from competition. *This interpretation of subsection C.08.004.01(1) is consonant with section 5 and 6 of Article 1711 of the NAFTA.*³⁵

By changing the wording of C.08.004.1 to “codify more clearly Canada’s data protection commitments” as the RIAS states, the government appears to have decided that the Federal Court of Appeal was wrong in *Bayer* when it held that the existing section, and the Minister’s interpretation of it, is in compliance with NAFTA.

Recent challenges to the new Food and Drug Regulations

After the amendments, generic manufacturers launched two judicial review applications challenging the amendments: *Apotex v. Canada (Attorney General)*,³⁶ and *Canadian Generic Pharmaceutical Association (CGPA) v. Canada (Attorney General)*,³⁷ the latter brought by CGPA, an industry association representing generic drug manufacturers in Canada, in which I represent the CGPA.

In these cases, generic manufacturers argue the so-called “data protection” amendments are outside the federal government’s power to pass regulations because they are not authorized by the *Food and Drugs Act*. The Act only authorizes regulations “deemed

³⁵ *Bayer*, supra, at para. 12.

³⁶ Federal Court File No. T-2047-06.

³⁷ Federal Court File No. T-1976-06.

necessary” for the implementation of NAFTA and TRIPS. However, argues the generic industry, the new regulations cannot be deemed necessary to implement NAFTA or TRIPS because they go well beyond both. Canada’s previous regime was held by the Federal Court of Appeal in *Bayer* to comply with Canada’s international treaty obligations.

The new regulations impose a term of data protection which is more than what is required by NAFTA. NAFTA only provides for five years of data protection while the new regulations call for eight.

Furthermore, NAFTA only requires that confidential data not be disclosed or relied on. However, the new regulations prohibit a generic manufacturer from seeking regulatory approval for a product even though neither it nor the Minister relies on innovator data when the generic submission is processed by Health Canada, as confirmed by the *Bayer* case. No trade secrets are revealed to anyone in the course of reviewing a generic submission. Rather, the generic manufacturer does a bioequivalence study against the innovator’s physical drug which is openly sold in the market. The innovator, of course, does not keep confidential that its drug has been found to be safe and effective.

In addition, generic manufacturers argue the new regulations are not within the constitutional power of the federal government. While purportedly enacted under the *Food and Drugs Act*, they have nothing to do with health and safety. Rather, the purpose

of the regulations is the protection of confidential information, a matter of provincial jurisdiction.

The Attorney General of Canada brought preliminary motions this spring to strike both of these proceedings, arguing that both CGPA and Apotex lack standing to challenge the regulations. One judge of the Federal Court struck out Apotex's application for judicial review³⁸ but another judge dismissed the Attorney General's motion, and declined to strike CGPA's application.³⁹ Both decisions are currently under appeal.

Conclusion

As I stated earlier, about 46% of prescriptions are filled with generic drugs in Canada versus about 63% in the US. Will the recent changes affect this 46% number and if so how?

The "data protection" regulations clearly create a new legally sanctioned form of monopoly, and if not struck down, will slow the introduction of generic drugs to the market. The changes to the NOC Regulations, and the potential effect of the AstraZeneca decision, may balance this effect but this is unclear. On balance, it seems unlikely the overall effect of all these changes will be to increase the number of prescriptions filled by generic drugs, or to alleviate concerns as to the overall spending in Canada on prescription drugs to any significant degree.

³⁸ 2007 FC 232.

³⁹ 2007 FC 154.

Serious changes may have to be made to the system one day, as fiscal pressures grow.

But that day has not yet come.