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IP UPDATE

CANADIAN PHARMACEUTICAL INTELLECTUAL PROPERTY LAW NEWSLETTER

Canadian Parliament Approves Legislation to Permit Exports of Patented Pharmaceuticals to Developing Countries

On May 14, 2004, Parliament approved Bill C-9, *An Act to amend the Patent Act and the Food and Drugs Act (The Jean Chrétien Pledge to Africa Act)*, making Canada the first country to implement the Decision of the World Trade Organization (WTO) General Council of August 30, 2003. The Decision implements paragraph 6 of the Doha Declaration on the TRIPS Agreement and Public Health and allows any member country to export pharmaceuticals made under compulsory licences within the terms set out in the Decision.

The stated purpose of the Bill is "to facilitate access to pharmaceutical products to address public health problems afflicting many developing and least-developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics." The Bill permits exports of fifty-six defined products (see **Table A**[1]) and permits exports to all WTO countries plus all non-WTO least-developed countries (LDCs), except the 23 WTO countries that have opted out. Apart from the requirement that the generic manufacturer must effectively obtain Canadian regulatory approval, it will not be difficult to obtain a compulsory licence under the system. The Bill does not grant patentees any opportunity to provide submissions to the Commissioner regarding the appropriateness of the grant of a licence, but does provide patentees with some protection from potential abuses of the system. The system is described in more detail below.

Schedules of Products and Eligible Importing Countries

The Bill has four schedules. **Schedule 1** lists the only products for which a compulsory licence may be issued (see **Table A**[1], which omits dosage form/strength restrictions included in Schedule 1). The products are primarily based on the WHO Model List of Essential Medicines and comprise antiretrovirals (ARV, *i.e.* drugs to treat HIV/AIDS), as well as drugs to treat a whole host of other conditions, including tuberculosis, malaria, antibiotics (*e.g.* ciprofloxacin), anti-cancer drugs (*e.g.* doxorubicin), and cardiovascular drugs (*e.g.* enalapril). A drug may be added if it "may be used to address public health problems... especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics" and if it is considered appropriate to do so.

Schedules 2, 3 and 4 list the eligible importing countries. **Schedule 2** lists all LDCs, both WTO and non-WTO. These countries need not establish insufficient manufacturing capacity in order to import under the System. **Schedule 4** lists the WTO countries that have agreed to use the system as importers only in situations of national emergency or other circumstances of extreme urgency. **Schedule 3** lists all WTO countries that are not in Schedules 2 and 4, and that have not opted out of the system. Countries may be added to or removed from the Schedules by Order of the Governor in Council. For example, non-WTO developing countries may be added to Schedule 4 in defined circumstances.

Process to Obtain Compulsory Licence

An application must be filed with the Commissioner of Patents and must include: the name of the product; the quantity; the name of the relevant patent number(s) and patentee(s); the name of the importing country;

[1] Please see page 4 of this newsletter.

and the name of the governmental person or entity, or the person or entity permitted by the government of the importing country, to which the product is to be sold.

The applicant must also provide the Commissioner with (1) confirmation that it had sought a voluntary licence from the patentee(s) on reasonable terms and conditions and that such efforts had not been successful and (2) a copy of the various notices required by the Decision to be made by the importing country, including, for WTO countries, the notices provided to the TRIPS council[2]:

- specifying the name of the product and the quantity needed;
- confirming that the product is not patented in the importing country or, where the product is patented, that the importing country has granted or intends to grant a compulsory licence for that product;
- for Schedule 3 and 4 countries, stating that the importing country has insufficient or no manufacturing capacity for the product; and
- for Schedule 4 countries, stating that the importing country is faced with a national emergency.

Apart from Health Canada approval, there are few requirements under the Bill to obtain a compulsory licence. Further requirements may be found in the *Regulations*. If these requirements are met, the Commissioner has no discretion to refuse a licence, i.e. he "shall... authorize the person to make, construct and use a patented invention solely for the purposes directly related to the manufacture of the pharmaceutical product named in the application and to sell it for export."

The product must meet Canadian standards for safety and efficacy and also, must meet the regulations relating to the marking, embossing, labeling and packaging that identify the product as having being manufactured in Canada as permitted by the Decision and in a manner that distinguishes it from the innovator's version of the pharmaceutical product sold in Canada.

The Compulsory Licence

The terms and conditions of the licence include:

1. Use (a) must be limited to a specific quantity and for use in a specific country and (b) is non-exclusive;
2. The licence is (a) valid for two years from the date of grant (but is renewable once for another two years if not all product authorized is exported) and (b) is non-transferable; and
3. The licensee must:
   (a) establish a website disclosing information relating to the licence, including the distinguishing features of its product and information identifying every known party that will be handling the product while it is in transit from Canada to the importing country;
   (b) pay a royalty determined in the prescribed manner;
   (c) provide the Commissioner and the patentee with a copy of its agreement with the buyer; and
   (d) before each shipment, provide the importing country and the buyer with an export notice.

Termination Provisions

The Bill provides a few automatic termination provisions, for example, a licence will terminate 30 days after the product at issue is removed from Schedule 1. There are also provisions permitting termination by the Federal Court for reasons including:

- the application for the compulsory licence contained any material information that is inaccurate;

[2] When made, these notices will be posted on the WTO website.

- the product exported has been, with the knowledge of the licensee, re-exported in a manner that is contrary to the Decision; and
- the product was exported, other than in the normal course of transit, to a country other than that authorized.

Finally, if the average price of the product is equal to or greater than 25 per cent of the average price in Canada for the patentee's product, the patentee may apply to the Federal Court for an order terminating the licence or requiring the licensee to pay compensation to the patentee on the basis that the essence of the agreement is "commercial in nature." The Court will determine whether the agreement is commercial in nature based on factors including "the need for the licensee to make a reasonable return sufficient to sustain a continued participation in humanitarian initiatives." If the average price does not exceed the direct supply cost of the product plus 15 per cent, the Court cannot terminate the licence.

Implications of the Bill for Patentees

Shortly after the Bill was first tabled, Canada's largest generic manufacturer, Apotex Inc., announced that it was prepared to produce a generic version of AZT for export under the system. However, the Canadian Generic Pharmaceutical Association (CGPA) has recently stated that "further amendments are required to realize generic participation in this particular initiative," pointing to "potential court battles" relating to the termination provision if the agreement is commercial in nature and royalty payments. The CGPA has also taken issue with the two-year limitation on licences, stating: "After a generic company has spent three to five years and millions of dollars developing a product, it should sell it for as long as they can attract buyers with low prices."

Assuming that the Canadian generic companies will use the system, the question is whether the Bill provides adequate safeguards to ensure that licences are granted only for humanitarian purposes and that the potential for diversion is minimized. It must be noted that the potential for diversion is significant: before the Standing Committee, Rx&D, the organization representing Canada's research-based pharmaceutical companies, provided specific historical examples of diversion including that "in 2002, more than 41,000 packages of HIV/AIDS medicines sold at not-for-profit prices and exported to several African countries by GlaxoSmithKline were intercepted in Antwerp and were destined for sale in the Belgian, Swiss and other EU markets."

Participation by Patentees Before Compulsory Licence Issues

The Bill permits minimal involvement by the patentee before a compulsory licence issues. Patentees will be aware of requests for product by WTO countries as the Bill requires that applications be tied to the notices, requesting product, that will be posted on the WTO website. Patentees will therefore be in a position at this time to assess whether to sell the product themselves. For non-WTO countries, the first time that patentees may become aware of a need for product will be a request by the generic for a voluntary licence. At that time, the generic must provide the patentee with the name of the buyer, so it may be possible to negotiate an agreement for sale by the patentee at that time.

If the patentee does not agree to sell the product or enter into a voluntary licence, the patentee will not have any control over whether a licence will issue as it does not have the right to make representations. Thus, by way of example only, if a Schedule 3 country requests drug X, the patentee would have no right to submit that the country indeed had sufficient manufacturing capacity for drug X and that the licence should not issue.

Participation by Patentees After Compulsory Licence Issues

The patentee will receive a notice in writing of the issuance of a compulsory licence, without delay. Also, the licensee's website will disclose information relating to the licence. Finally, before each shipment, the

patentee will be notified of the quantity to be exported and every known party that will be handling the product while it is in transit from Canada to the importing country, to facilitate product tracking. The patentee will have the ability to challenge the royalty rate in the Federal Court. The patentee may also seek to terminate the licence under certain circumstances, including on the basis that the agreement is "commercial in nature" or if product is re-exported with the knowledge of the licensee. However, knowledge may be difficult to establish. Furthermore, any termination by the Federal Court will likely take significant time.

Both the humanitarian efforts of Bill C-9 and the current text of the Bill have been supported by Rx&D. While the inability to make representations is significant, the balance of the controls in place, after issuance of the licence, may provide adequate protection. However, whether potential abuses will in fact be avoided obviously remains to be seen.

What Happens Next

Bill C-9 will come into effect once the regulations under the Bill have been passed, likely this Fall. A review of the amendments and their application must be completed by the Minister within two years after they come into force. While it is not yet clear whether the system will actually be used by the Canadian generic industry, the public will become aware of any applications as they will be posted on the Canadian Intellectual Property Office website. We will report on further developments in future issues of *Rx IP Update*.

Nancy P. Pei

TABLE A: Schedule 1 to Bill C-9 with dosage form limitations omitted*

abacavir (ABC)
abacavir + lamivudine + zidovudine
aciclovir
amphotericin B
amprenavir
azithromycin
beclometasone
ceftazidime
ceftriaxone
ciclosporin
ciprofloxacin
ciprofloxacin hydrochloride
daunorubicin
delavirdine
didanosine (ddI)
diphtheria antitoxin
diphtheria vaccine
doxorubicin
efavirenz (EFV or EFZ)
eflornithine
enalapril
erythromycin
etoposide
factor IX (complex coagulation factors II, VII, IX, X) concentrate
hepatitis B vaccine
ibuprofen
indinavir (IDV)
insulin injection (soluble)
intermediate-acting insulin
isoniazid + pyrazinamide + rifampin
ivermectin
lamivudine (3TC)
lamivudine + zidovudine
levodopa + carbidopa
levofloxacin
lithium carbonate
lopinavir + ritonavir (LPV/r)
metoclopramide
metronidazole
morphine
nelfinavir (NFV)
nevirapine (NVP)
nifedipine
nitrofurantoin
ofloxacin
potassium chloride
ranitidine
ritonavir
salbutamol
saquinavir (SQV)
stavudine (d4T)
testosterone
timolol
verapamil
zalcitabine
zidovudine (ZDV or AZT)

* Please refer to Schedule 1 to Bill C-9 for dosage form restrictions

Supreme Court of Canada Proceedings

Decisions

Percy Schmeiser v. Monsanto Canada (**glyphosate-resistant canola (ROUNDUP READY CANOLA)**), May 21, 2004

The Supreme Court has dismissed, in part, Mr. Schmeiser and Schmeiser Enterprises' appeal of a Federal Court of Appeal decision, dismissing their appeal from a trial judge's decision. The trial judge had found that the appellants had infringed Monsanto's patent by planting a crop of glyphosate-resistant canola having a gene or cell that is the subject of the patent. The trial judge granted Monsanto an injunction and the defendants' profits. The decision is described in the May 21, 2004 edition of *IP Update*.

Full Judgment (2004 SCC 34)

Leave Applications

Janssen-Ortho v. The Minister of Health (**fentanyl transdermal patch (DURAGESIC)**), April 13, 2004

Janssen-Ortho has filed a leave application from a Federal Court of Appeal decision, upholding a decision to remove a patent from the Patent Register on the basis that the DURAGESIC patch (in particular, the release membrane, the drug reservoir, and the backing) does not fall within the definition of "medicine" for the purposes of the *Regulations*. The Court of Appeal judgment was reported in the March 2004 issue of *Rx IP Update*. Janssen-Ortho's application for a stay of the Court of Appeal's decision pending appeal has been dismissed.

Court of Appeal Decision (2004 FCA168)

AstraZeneca and Merck v. Apotex (**lisinopril (APO-LISINOPRIL, ZESTRIL, PRINIVIL)**), May 7, 2004

The Supreme Court has dismissed Apotex' application for leave to appeal a Federal Court of Appeal decision, which denied Apotex leave to amend its statement of defence, to withdraw an admission of infringement. The Court of Appeal judgment was reported in the January 2004 issue of *Rx IP Update*.

Recent Court Decisions

Patented Medicines (Notice of Compliance) Regulations

Novartis v. RhoxalPharma (**cyclosporine (NEORAL)**), March 29, 2004

Judge grants application for an Order of prohibition. RhoxalPharma had alleged non-infringement. Judge construes the relevant claim differently from that of a judge in a previous proceeding under the *Regulations*, in view of different evidence presented. RhoxalPharma has appealed.

Full Judgment (2004 FC 474)

Apotex v. AstraZeneca (**omeprazole (LOSEC)**), April 30, 2004

Judge dismisses Apotex' application for declarations that if the patent at issue is eligible for listing on the Patent Register, it is eligible for listing only in respect of a specific new drug submission and that Apotex is not required to address the patent. Apotex argued, in part, that at the time Apotex filed its submissions for Apo-Omeprazole and at the time the submission became approvable, AstraZeneca was not marketing LOSEC pursuant to a Notice of Compliance (NOC) for the new uses of the patent and therefore Apotex was not required to address the patent. Judge finds that the issues raised by Apotex should have been dealt with pursuant to a section 6(5)(a) application for dismissal and in any event, rejects Apotex' arguments on the merits. Apotex has appealed.

Full Judgment (2004 FC 650)

AstraZeneca v. The Minister of Health (**omeprazole (LOSEC)**), May 20, 2004

Judge dismisses application for an Order requiring the Minister to add a patent to the Patent Register. The patent list was filed in connection with a Supplemental New Drug Submission (SNDS), filed in connection with a company name change, within 30 days of patent issuance. Judge finds that the relevant submission is "something other than a New Drug Submission (NDS), Abbreviated New Drug Submission (ANDS) or Supplemental New Drug Submission," characterizing it as "an administrative SNDS" and that this was insufficient for the purpose of accepting the patent list. AstraZeneca has filed a motion for reconsideration.

Full Judgment (2004 FC 736)

Other Decisions

Torpharm v. Commissioner of Patents (**lisinopril (ZESTRIL, PRINIVIL)**), May 7, 2004

Judge allows Torpharm's appeal of a Commissioner of Patents decision, rejecting Torpharm's application for a compulsory licence to acquire bulk lisinopril and manufacture tablets for export. Torpharm had alleged abuse of patent rights. Judge remits the matter to the Commissioner for reconsideration.

Full Judgment (2004 FC 673)

Health Canada News

The Therapeutic Products Directorate has released a statistical overview relating to the administration of the *Regulations*. The report provides statistics relating to (i) the maintenance of the Patent Register (number of patent lists filed, number of patent lists accepted and rejected, and litigation resulting from the acceptance or rejection of patents for listing on the Patent Register) and (ii) the requirements for second persons to address patents listed on the Patent Register (number of notices of allegation served, number of prohibition applications commenced and outcomes of the applications).

Statistical Report 2003 *Patented Medicines (Notice of Compliance) Regulations*

Patented Medicines Prices Review Board (PMPRB) Matters

On May 6, 2004, the PMPRB accepted a voluntary compliance undertaking (VCU) from Leo Pharma for alfacalcidol (ONE-ALPHA).

VCU Notice

On August 23, 2004 the PMPRB will hold a hearing to determine whether Sanofi-Synthelabo is selling or has sold rasburicase (FASTURTEC) at an excessive price and if so, what order, if any, should be made. Applications for leave to intervene must be filed by June 11, 2004.

Hearing Notice

New Court Proceedings

Patented Medicines (Notice of Compliance) Regulations

Medicine: **fosinopril sodium (MONOPRIL)**
Applicants: Bristol-Myers Squibb Canada Co and Bristol-Myers Squibb Company
Respondents: Pharmascience Inc and The Minister of Health
Date Commenced: April 5, 2004
Comment: Application for Order of prohibition until expiry of Patent No. 2,019,324. Pharmascience alleges non-infringement.

Medicine: **paroxetine hydrochloride controlled release tablets (PAXIL CR)**
Applicant: GlaxoSmithKline Inc
Respondents: Attorney General of Canada and The Minister of Health
Date Commenced: April 28, 2004
Comment: Application for order directing the Minister to add Patents Nos. 1,298,479 and 2,031,393 to the Patent Register.

Medicine: **paroxetine hydrochloride controlled release tablets (PAXIL CR)**
Applicant: GlaxoSmithKline Inc
Respondents: Attorney General of Canada and The Minister of Health
Date Commenced: April 28, 2004
Comment: Application for order directing the Minister to add Patents Nos. 1,298,479 and 2,031,393 to the Patent Register.

Medicine: **clarithromycin (BIAXIN BID)**
Applicants: Abbott Laboratories and Abbott Laboratories Limited
Respondents: Pharmascience Inc and The Minister of Health
Date Commenced: April 29, 2004
Comment: Application for Order of prohibition until expiry for Patents Nos. 2,277,274; 2,386,527; 2,386,534; 2,387,356 and 2,386,361. Pharmascience alleges non-infringement.

Medicine: **ramipril (ALTACE)**
Applicants: Aventis Pharma Inc and Aventis Deutschland GmbH
Respondents: Pharmascience Inc and The Minister of Health
Date Commenced: April 29, 2004
Comment: Application for Order of prohibition until expiry of Patent No. 2,023,089. Pharmascience alleges non-infringement and invalidity.

Medicine: **amlodipine besylate (NORVASC)**
Applicants: Pfizer Canada Inc and Pfizer Limited
Respondents: Ratiopharm Limited and The Minister of Health
Date Commenced: April 30, 2004
Comment: Application for Order of prohibition until expiry of Patent No. 1,321,393. Ratiopharm alleges non-infringement and invalidity.

Medicine: **rofecoxib (VIOXX)**
Applicant: Merck Frosst Canada & Co
Respondents: Merck & Co Inc, Novopharm Limited and The Minister of Health
Date Commenced: April 30, 2004
Comment: Application for Order of prohibition until expiry of Patent No. 2,254,061. Novopharm alleges that certain claims are irrelevant to Novopharm's submission, non-infringement and invalidity.

Medicine: **norelegestromin/ethinyl estradiol transdermal system (EVRA)**
Applicant: Janssen-Ortho Inc
Respondents: The Attorney General of Canada and The Minister of Health
Date Commenced: May 4, 2004
Comment: Application for Order quashing the decision of the Minister, refusing to add Patent No. 2,222,133 to the Patent Register.

Medicine: **fenofibrate (LIPIDIL SUPRA)**
Applicants: Fournier Pharma Inc and Laboratoires Fournier SA
Respondents: Apotex Inc and The Minister of Health
Date Commenced: May 7, 2004
Comment: Application for Order of prohibition until expiry of Patent No. 2,372,576. Apotex alleges non-infringement.

Medicine: **ondansetron (ZOFRAN ODT)**
Applicants: GlaxoSmithKline Inc and Glaxo Wellcome Inc
Respondents: Novopharm Limited and The Minister of Health
Date Commenced: May 18, 2004
Comment: Application for Order of prohibition until expiry of Patent No. 2,205,600. Novopharm alleges non-infringement.

Medicine:	**azithromycin (ZITHROMAX)**
Applicants:	Pfizer Canada Inc and Pfizer Inc
Respondents:	Pharmascience and The Minister of Health
Date Commenced:	May 20, 2004
Comment:	Application for Order of prohibition until expiry of Patent No. 1,314,876. Pharmascience alleges non-infringement and that the patent is not properly listed on the Patent Register.

Medicine:	**ursodiol (URSO)**
Applicant:	Axcan Pharma Inc
Respondents:	Pharmascience Inc and The Minister of Health
Date Commenced:	May 20, 2004
Comment:	Application for Order of prohibition until expiry of Patent No. 1,318,590. Pharmascience alleges invalidity.

Medicine:	**mycophenolate sodium delayed-release tablets (CELLCEPT)**
Applicant:	Hoffmann-LaRoche Limited
Respondents:	Syntex (U.S.A.) Inc, Novartis Pharmaceuticals Canada Inc and The Minister of Health
Date Commenced:	May 21, 2004
Comment:	Application for Order of prohibition until expiry of Patent No. 1,333,285. Novartis alleges invalidity.

Other New Proceedings

Medicine:	**quinine (APO-QUININE)**
Applicant:	Apotex Inc
Respondent:	The Minister of Health
Date Commenced:	April 30, 2004
Comment:	Application for Order compelling the Minister to issue Apotex DINs for Apo-Quinine.

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