SMART & BIGGAR | FETHERSTONHAUGH MAY 2006

Rx IP UPDATE

CANADIAN PHARMACEUTICAL INTELLECTUAL PROPERTY LAW NEWSLETTER

Lisinopril Patent Valid and Infringed by Apotex

On April 26, 2006, a trial judge of the Federal Court found that the lisinopril patent (No. 1,275,350) is valid and that it has been infringed by Apotex (*Merck and AstraZeneca v. Apotex*, 2006 FC 524).

This patent infringement action was brought by Merck (patentee and certain related companies) and AstraZeneca (licensee) against Apotex in 1996. The parties sell lisinopril in Canada under the trademarks Apo-Lisinopril, ZESTRIL (AstraZeneca) and PRINIVIL (Merck).

Infringement

Apotex had admitted infringement but raised four defences relating to certain quantities. The Judge rejected the arguments based on section 56 of the *Patent Act* and a compulsory licence that had been extinguished.

However, he found that certain quantities were exempt in view of section 55.2(1) of the *Patent Act*, which provides:

> 55.2 (1) It is not an infringement of a patent for any person to make, construct, use or sell the patented invention solely for uses reasonably related to the development and submission of information required under any law of Canada, a province or a country other than Canada that regulates the manufacture, construction, use or sale of any product.

The Judge found that lisinopril quantities used for the purpose of obtaining regulatory approval were exempt, including those that were not referenced in the submissions but were in one way or another directed to that purpose. The Judge additionally found that material routinely taken by Apotex as samples from incoming raw material and of the finished products, stored in the event that they are required for future reference in accordance with regulatory requirements, were also exempt.

Finally, the Judge found that Apotex's use of lisinopril in ongoing research and development of alternate formulae, alternate techniques for tablet making and the like, falls within a "fair dealing" exemption to infringement.

Validity

The '350 patent issued on October 16, 1990 from a voluntary divisional application filed on August 1, 1989 from a parent application filed in Canada on December 6, 1979.

Apotex argued that the patent was invalid on three bases: 1. It issued from an improper divisional application; 2. double patenting in view of an earlier issued patent relating to a combination of enalapril and hydrochlorothiazide; and 3. wilful delay by Merck in prosecution of the application.

The Judge held that Apotex was estopped from raising these validity attacks in view of prior litigation involving Apotex, Merck and another patent directed to enalapril. The Judge held that the same attacks could have been raised in the earlier litigation since the enalapril patent arose from the same parent application and issued on the same day as the lisinopril patent.

The Judge nonetheless dealt with the validity attacks on the merits.

On the improper divisional attack, the Judge rejected Apotex's argument that the parent application did not both describe and claim more than one invention, *i.e.* that it only described one invention, the class, of which lisinopril was but an example. He also held that even if several patents claiming the same invention had been granted, a sufficient remedy exists in the application of double patenting.

The double patenting attack was rejected as lisinopril and enalapril were found to be separate inventions.

Finally, the wilful delay attack was rejected on the basis of lack of evidence.

Apotex may appeal, as of right.

Nancy P. Pei

LOSEC Capsule "Marketed" Appeal Heard by Supreme Court of Canada

As reported in our October 2005 special issue of *Rx IP Update*, the Supreme Court of Canada granted leave to Apotex to appeal a Federal Court of Appeal decision which quashed its notice of compliance (NOC) for Apo-Omeprazole capsules. The Court of Appeal's decision turned on the interpretation of the "marketed" requirement in section 5(1) of the *Patented Medicines (Notice of Compliance) Regulations* ("*Regulations*"). Section 5(1) prescribes the requirements that must be met before a second person is required to address patents on the Patent Register.

The appeal was heard on May 11, 2006, and was taken under reserve by the Court. Canada's Research-Based Pharmaceutical Companies (Rx&D) and the Canadian Generic Pharmaceutical Association (CGPA) intervened.

Ontario Bill to Amend Formulary Legislation Referred to Standing Committee

As reported in our April 2006 issue of *Rx IP Update*, the Ontario Government introduced Bill 102, the *Transparent Drug System for Patients Act, 2006* on April 13, 2006. The legislation, if passed, will result in far-reaching changes to the *Drug Interchangeability and Dispensing Fee Act* and the *Ontario Drug Benefit Act*. The Bill has passed second reading and was referred to the Standing Committee on Social Policy on May 10, 2006. The Committee must finish its consideration and file amendments to the Bill on June 6, 2006 and report the Bill back to the House not later than June 7, 2006. Once the Bill is reported, it will be ordered for a third reading. As previously reported, under the current Bill, most of the amendments, if passed, would come into force on October 1, 2006.

PMPRB Rules Price of a Combination Medicine (Dovobet) Excessive

On April 19, 2006, the Patented Medicine Prices Review Board (PMPRB) issued its decision (PMPRB-04-D2-DOVOBET) ruling that LEO Pharma is selling and has sold DOVOBET (calcipotriol (DOVONEX)/ betamethasone dipropionate (DIPROSONE)) in Canada at an excessive price.

The Board compared the price to the combined prices of DOVONEX and DIPROSONE, finding that "the definition of any therapeutic class for price comparison purposes requires, and absent sound evidence to the contrary, the active ingredients of a combination medicine, if sold as separate medicines in Canada, constitute the most appropriate – and indeed uncommonly compelling – therapeutic class for price comparison purposes". The Board held that the "sound evidence to the contrary" must be "reliable evidence", from *e.g.* "a properly structured and administered trial", "that the combination medicine provides a material advantage over the medicines that contain its active ingredients…. To be material, the difference in clinical effectiveness would have to be at least statistically significant and therapeutically relevant".

The Board concluded that the evidence established that the appropriate dosage regimen for the comparison of DOVOBET to DOVONEX plus DIPROSONE is a "gram-to-gram" comparison applicable to medicines that treat chronic disease, as is the case here, instead of a "course of treatment" comparison applicable to medicines used to treat an acute condition.

The Board ordered LEO Pharma to return the excessive revenues that it has collected on the sale of DOVOBET in Canada.

Recent Court Decisions

Patented Medicines (Notice of Compliance) Regulations

Axcan Pharma v. Pharmascience (**ursodeoxycholic acid (URSO)**), April 26, 2006

Judge dismisses Axcan's application for an Order of prohibition, finding Axcan's patent invalid as claiming a method of medical treatment or, alternatively, was previously disclosed.

Full Judgment (2006 FC 527)

New Court Proceedings

Patented Medicines (Notice of Compliance) Regulations

Medicine: **raloxifene hydrochloride (EVISTA)**
Applicant: Eli Lilly Canada Inc
Respondents: Apotex Inc, The Minister of Health and Eli Lilly and Company
Date Commenced: March 1, 2006
Court File No: T-361-06
Comment: Application for Order of prohibition until expiry of Eli Lilly's Patent No 2,250,191. Apotex alleges non-infringement.

Medicine: **lansoprazole (PREVACID)**
Applicants: Abbott Laboratories Limited and Tap Pharmaceuticals Inc
Respondents: Takeda Pharmaceutical Company Limited, Apotex Inc and The Minister of Health
Date Commenced: March 31, 2006
Court File No: T-585-06
Comment: Application for Order of prohibition until expiry of Takeda's Patent No 2,009,741. Apotex alleges non-infringement, invalidity, and that the patent is not eligible for listing on the Patent Register.

Medicine: **amlodipine besylate (NORVASC)**
Applicants: Pfizer Canada Inc and Pfizer Inc
Respondents: Ratiopharm Inc and The Minister of Health
Date Commenced: March 31, 2006
Court File No: T-586-06
Comment: Application for Order of prohibition until expiry of Patent No 2,355,493. Ratiopharm alleges non-infringement, invalidity, and that the patent is not eligible for listing on the Patent Register.

Medicine: **pantoprazole (PANTOLOC)**
Applicants: Solvay Pharma Inc and Altana Pharma AG
Respondents: Cobalt Pharmaceuticals Inc and The Minister of Health
Date Commenced: April 6, 2006
Court File No: T-604-06
Comment: Application for Order of prohibition until expiry of Altana's Patents Nos 1,254,215, 2,089,748, 2,092,694 and 2,109,697. Cobalt alleges non-infringement ('748, '694 and '697 patents) and accepts that the NOC will not issue until expiry of the '215 patent.

Medicine: **amlodipine besylate (NORVASC)**
Applicants: Pfizer Canada Inc and Pfizer Inc
Respondents: Apotex Inc and The Minister of Health
Date Commenced: April 13, 2006
Court File No: T-659-06
Comment: Application for Order of prohibition until expiry of Patent No 2,355,493. Apotex alleges non-infringement, invalidity, and that the patent is not eligible for listing on the Patent Register.

Medicine: **amlodipine besylate (NORVASC)**
Applicants: Pfizer Canada Inc and Pfizer Inc
Respondents: Genpharm Inc and The Minister of Health
Date Commenced: April 13, 2006
Court File No: T-660-06
Comment: Application for Order of prohibition until expiry of Patents Nos 1,321,393 and 2,355,493. Genpharm alleges non-infringement and invalidity for both patents and also alleges that the '493 is not eligible for listing on the Patent Register.

Medicine: **mixed salts amphetamines (ADDERALL XR)**
Applicant: Shire Biochem Inc
Respondent: Patented Medicine Prices Review Board and Attorney General of Canada
Date Commenced: April 13, 2006
Court File No: T-666-06
Comment: Urgent application for judicial review of decision by the PMPRB denying Shire's request for a short adjournment of the evidentiary aspect of a hearing to be held under section 83 of the *Patent Act*.

OTTAWA

55 Metcalfe Street, Suite 900
P.O. Box 2999, Station D
Ottawa, Ontario Canada
K1P 5Y6
t. 613.232.2486
f. 613.232.8440

ottawa@smart-biggar.ca

TORONTO

438 University Avenue
Suite 1500, Box 111
Toronto, Ontario Canada
M5G 2K8
t. 416.593.5514
f. 416.591.1690

toronto@smart-biggar.ca

MONTREAL

1000 de La Gauchetière St. W.
Suite 3300
Montreal, Québec Canada
H3B 4W5
t. 514.954.1500
f. 514.954.1396

montreal@smart-biggar.ca

VANCOUVER

650 West Georgia Street
Suite 2200
Box 11560, Vancouver Centre
Vancouver, B.C. Canada
V6B 4N8
t. 604.682.7780
f. 604.682.0274

vancouver@smart-biggar.ca

www.smart-biggar.ca

Other Proceedings

Medicine:	**homeopathic product (A. Vogel Sinna Comprimés)**
Applicant:	Bioforce Canada Inc
Respondents:	Madame Francine Ménard et Monsieur Stéphane Gélinas, Ministre de la Santé, Le Procureur Général du Canada
Date Commenced:	March 23, 2006
Court File No:	T-530-06
Comment:	Application for judicial review of the Minister of Health's decision, ordering the withdrawal of A. Vogel Sinna Comprimés from the market.

Contact Info

For more information, or to request a copy of any decision, pleading or legislation, please contact:

Gunars A. Gaikis
ggaikis@smart-biggar.ca

J. Sheldon Hamilton
jshamilton@smart-biggar.ca

Nancy P. Pei (Editor)
nppei@smart-biggar.ca

Pharmaceutical Practice Group

James D. Kokonis, Q.C., B.A.Sc. (Metallurgy), LL.B.
John R. Morrissey, B.Eng. (Elec.Eng.), S.M., LL.B.
Joy D. Morrow, B.Sc., M.Sc. (Cell Bio.), LL.B.
Michael D. Manson, B.Sc. (Bio.), Dipl.Ed., LL.B.
Tokuo Hirama, B.Sc., M.Sc. (Chem.)
J. Christopher Robinson, B.Sc., M.Sc. (Genetics), LL.B.
Steven B. Garland, B.Eng. (Chem.-Biochem.Eng.), LL.B.
David E. Schwartz, B.Sc. (Genetics), LL.B.
Yoon Kang, B.Sc., M.Sc. (Molec.Bio. & Genetics), LL.B.
Geneviève M. Prévost, B.Sc. (Chem.), LL.B.
Jeremy E. Want, B.Sc. (Chem.), LL.B.
Daphne C. Ripley, B.Sc., M.Sc. (Chem.), LL.B.
Denise L. Lacombe, B.Sc. (Chem.), M.Sc. (Chem.Phys.), LL.B.
James Jun Pan, B.Eng. (Eng.Phys.), Ph.D. (Chem.), LL.B.
Jennifer L. Ledwell, B.Sc. (Biochem.), Ph.D. (Molec. & Cell Physio.)
Y. Lynn Ing, B.Sc. (Biochem.), Ph.D. (Molec.Bio.), J.D.
Junyi Chen, B.A. (Chem.), M.Sc. (Chem.), Ph.D. (Chem.), J.D.
A. David Morrow, B.Sc. (Physics), LL.B.
John Bochnovic, B.Eng. (Elec.Eng.), S.M., LL.B.
Gunars A. Gaikis, B.Sc.Phm., LL.B.
Keltie R. Sim, B.Sc. (Mycology), LL.B.
Mark K. Evans, B.Sc., LL.B.
Solomon M.W. Gold, B.Sc., M.Sc. (Bio.), LL.B.
J. Sheldon Hamilton, B.A.Sc. (Chem.Eng.), LL.B.
Brian G. Kingwell, B.Sc. (Biochem.), M.Sc. (Molec. Cell Bio.), LL.B.
Nancy P. Pei, B.Sc.Phm., LL.B.
Thuy H. Nguyen, B.Sc., Ph.D. (Biochem.)
Colin B. Ingram, B.A.Sc. (Elec.Eng.), LL.B.
Sally A. Hemming, B.Sc., Ph.D. (Biochem.), J.D.
May Ming Lee, B.Sc.Phm., LL.B.
Scott A. Beeser, B.Sc. (Biochem.) Ph.D. (Bio.), LL.B.
T. Nessim Abu-Zahra, B.Sc. (Life Sci.), M.Sc. (Pharmacology), J.D.
Daniel M. Anthony, B.Sc. (Cell Bio. & Genetics), J.D.

SMART & BIGGAR
FETHERSTONHAUGH