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IP UPDATE

CANADIAN PHARMACEUTICAL INTELLECTUAL PROPERTY LAW NEWSLETTER

Allegation of Invalidity for Paroxetine Formulation Patent Justified

The Federal Court of Appeal, in a decision under the *Patented Medicines (Notice of Compliance) Regulations*, has upheld a Trial Division decision ruling that an allegation of invalidity made by Apotex was justified on the basis of anticipation. The patent in issue (the "'637 patent"), owned by SmithKline Beecham ("SmithKline"), covered a paroxetine tablet made using a process in which water is absent, thereby avoiding a "pink hue" problem encountered during formulation.

Apotex asserted that the '637 patent was anticipated by an earlier SmithKline patent for crystalline paroxetine hydrochloride hemihydrate (the "'060 patent"). The '060 patent disclosed that compositions of the invention "may be formulated by conventional methods of admixture such as blending, filling and compressing." Apotex also alleged that the '637 patent was obvious. The Trial Division Judge found the allegation of invalidity based on anticipation to be justified, although he rejected the allegation of invalidity based on obviousness. The Trial Division Judge found that a skilled person, having determined that wet formulation of paroxetine gives rise to a "pink hue problem", would have sought at least a partial solution. The Trial Judge further found that a logical first step would be to turn to alternative formulation techniques described in the '060 patent and determine whether "each or any of those alternative formulation techniques" would solve the problem.

On appeal, the Court noted that anticipation is a question of mixed fact and law and, as a result, in the absence of an error in law, the Court must afford considerable deference to the Trial Judge, only intervening if the findings of fact constituted a palpable and overriding error.

SmithKline argued that the earlier '060 patent taught a wide array of formulations beyond those covered by the '637 patent. As a result, the '060 patent did not inevitably teach the use of a formulation of paroxetine where water was absent. SmithKline relied upon the jurisprudence governing selection patents in which the Courts had previously upheld patents covering a selection of compounds (species) where the earlier patent covered a broader class (or genus). The invention in each of the selection cases was the recognition of an advantage to the selected compounds and the identification of those compounds.

The Court noted SmithKline's suggestion that "a claim to a specific chemical compound cannot be anticipated by a prior art reference that only teaches a broad genus of compounds into which the particular compound falls because the prior art reference does not give directions that inevitably result in the specific compound". In effect, the prior reference must lead to the later patented result in order to be anticipatory.

The Court rejected SmithKline's argument, distinguishing the selection patent cases on the basis that the particular selected compounds were not identified in the prior art and therefore the identification of the compound was novel and inventive. Since the prior art did not clearly and simply describe the latter invention, a further inventive step was required. The Court was not persuaded that the Trial Judge had erred by finding that there was no inventive step or skill to arrive at the '637 patent. The Court also distinguished the selection cases noting that the '637 patent merely verified properties of a known substance formulated using common techniques.

The decision of the Court of Appeal may have significant consequences for pharmaceutical patentees, particularly in cases where subsequent patents claim formulations or other forms of a known compound, such as polymorphs. The Court may have narrowed the scope of protection for formulations that employ known techniques to overcome development problems, at least where the cause of the problem can be readily identified. The decision also suggests that experimentation among known alternatives may be insufficient to sustain a patent because the Court of Appeal endorsed the Trial Judge's decision that a logical first step to solving the "pink hue" problem, identified as a result of wet formulation, would be to turn to the alternative formulation methods described in the '060 patent.

J. Sheldon Hamilton

Supreme Court of Canada Hearings

AstraZeneca AB v. *Novopharm* (**omeprazole capsules** (**LOSEC**)); *Ciba-Geigy* v. *Novopharm* (**diclofenac slow-release tablets** (**VOLTAREN SR**)), June 6, 2002

Court refuses AstraZeneca and Novartis (formerly Ciba-Geigy) leave to appeal Court of Appeal decision overturning the Registrar of Trade-marks' decision allowing trade-mark applications for colour applied to the surface of pharmaceutical tablet or capsule preparations. For more information, please see the November 2001 issue of *Rx IP Update*, where the Court of Appeal decision was reported and the January 2002 issue of *Rx IP Update*, where the application for leave was reported.

Supreme Court Bulletin

Apotex v. *Bayer* (**ciprofloxacin** (**CIPRO**)), June 13, 2002

Apotex' application for leave to appeal a decision prohibiting the Minister of Health from issuing a Notice of Compliance to Apotex is dismissed. One of the main issues in the case was whether a prior foreign patent application filed more than twelve months earlier and issued before the Canadian filing date was for the "same invention" so as to render the Canadian patent invalid.

Supreme Court Bulletin

Recent Court Decisions

Patented Medicines (Notice of Compliance) Regulations

Novartis v. *RhoxalPharma* (**cyclosporin** (**NEORAL**, **SANDIMMUNE**)), May 15, 2002

Court refuses to compel RhoxalPharma's affiant to answer a question about the timing of RhoxalPharma's New Drug Submission. The underlying affidavit was filed in support of RhoxalPharma's motion to have Novartis' application for prohibition dismissed on the basis that the application was redundant. The Court found that the timing of the submission was not relevant to this issue.

Full Judgment (*For a printer friendly version, please scroll down to the end of the Judgment)

Apotex v. *GlaxoSmithKline* (**paroxetine hydrochloride** (**PAXIL**)), May 28, 2002

GlaxoSmithKline unsuccessful in having Apotex' Notice of Application struck. In its Notice of Application, Apotex is seeking an order to require the Minister of Health to issue an NOC on the basis that its right to an NOC had vested prior to GlaxoSmithKline's addition of further patents to the patent list in respect of paroxetine hydrochloride. The Appellate Judge found that Apotex' review application is not so clearly improper as to be bereft of any possibility of success nor that the application is doomed due to an incurable defect.

Full Judgment (*For a printer friendly version, please scroll down to the end of the Judgment)

SmithKline Beecham v. *Apotex* (**paroxetine hydrochloride tablets** (**PAXIL**)), May 28, 2002

Court upholds the decision that SmithKline's formulation patent, solving the "pink hue" problem of its earlier patented formulations, lacks novelty in view of the earlier patent. Generic language in the body of the earlier patent specification relating to "conventional methods...[of]...blending, filling and compressing" was found to "provide all the information which, for practical purposes, is needed to produce the [invention] without the exercise of any inventive skill". For more information, please see the article on page one of this issue.

Full Judgment (Court of Appeal)

Full Judgment (Trial Division)

Hoffman-LaRoche v. *Apotex* (**naproxen slow-release tablets** (**NAPROSYN SR**)), May 28, 2002

Appeal of decision refusing to strike Apotex' Statement of Claim (reported in January 2002 issue of *Rx IP Update*) dismissed. Lower Court Judge had found that the motion to strike involved a question of interpretation of the *Regulations* and was a matter better left to the trier of the main case.

Full Judgment (Court of Appeal)

Full Judgment (Trial Division)

Novartis v. *Apotex* (**cyclosporin** (**NEORAL**)), June 13, 2002

Apotex successful on appeal in having Novartis' application for prohibition dismissed on the basis that it was an abuse of process. The lower level decision-maker had previously dismissed Apotex' case. The Appellate Judge, however, found that Novartis did not have an intention to prosecute the application and was using the application in order to delay the granting of an NOC to Apotex before an appeal in a related case could be disposed of. Novartis has appealed.

Full Judgment (*For a printer friendly version, please scroll down to the end of the Judgment)

GlaxoSmithKline v. *Pharmascience* (**paroxetine hydrochloride** (**PAXIL**)), June 17, 2002

Pharmascience ordered to produce portions of the Abbreviated New Drug Submission (ANDS), portions of the Drug Master File, the Product Monograph and samples (if provided along with the ANDS). Judge finds the information and samples to be relevant to the issue of non-infringement, as well as important and required for the effective disposition of the underlying prohibition application. Judge's conclusion is based in part on expert testimony that Pharmascience's tablets containing the anhydrate may convert to the hemihydrate, the subject of some patent claims.

Full Judgment (*For a printer friendly version, please scroll down to the end of the Judgment)

Other Decisions

Novopharm v. *Novartis* (**diclofenac sodium slow-release tablets** (**VOLTAREN SR**)), May 13, 2002

Court of Appeal dismisses Novopharm's appeal of a decision refusing to grant a restricted access confidentiality order in a reference to determine the nature of damages pursuant to an undertaking where an interlocutory decision was dissolved for delay. For a link to the lower court judgment, please see the October 2001 issue of *Rx IP Update*.

Full Judgment (*For a printer friendly version, please scroll down to the end of the Judgment)

Apotex v. *Merck* (**enalapril maleate** (**VASOTEC**)), May 28, 2002 and May 31, 2002

Court of Appeal upholds decision finding Apotex liable for patent infringement. In earlier proceedings, Apotex was found to infringe Merck's patent based on an acquisition of 44.9 kg of enalapril maleate from Delmar after Delmar's compulsory licence expired. In the current case, the Lower Court Judge held that the prior finding was determinative that Apotex' later acquisition of 772.9 kg of enalapril maleate from Delmar was also infringing (*res judicata* applied).

Within days of the appeal being allowed, the Lower Court Judge decided, *inter alia*, that Merck can elect between damages and an accounting of profits after having discovery of Apotex (with a discovery of Merck only following if an accounting is not elected) and that this is a case where punitive or exemplary damages are to be awarded, with the quantum of punitive damages to be determined following a determination of the general damages/profits. Apotex has appealed.

Full Judgment (Court of Appeal)

Full Judgment (Trial Division)

Full Judgment (Decision as to Remedy)

Ontario (Minister of Health) v. *Apotex* (**diltiazem hydrochloride slow-release capsule** (**APO-DILTIAZ CD**)), June 17, 2002

Ontario Court of Appeal reverses the decision overturning the Minister's decision not to increase the formulary listing price of Apo-Diltiaz CD. Apotex had written to the Minister requesting that the listed price of Apo-Diltiaz CD be reduced when a competitor's interchangeable drug product was to be listed in the formulary at a lower price. The competitor company subsequently requested that its listing be deleted. Apotex then sought to have its higher price restored. The Court of Appeal found that the Minister's decision was not patently unreasonable and should stand.

Full Judgment

New Federal Court Proceedings

Patented Medicines (Notice of Compliance) Regulations

Medicine: **Omeprazole** (**LOSEC**)
Applicant: Apotex Inc
Respondents: The Minister of Health, AstraZeneca AB and AstraZeneca Canada Inc
Date Commenced: May 23, 2002
Comment: Application for a declaration that AstraZeneca's Canadian Patent No. 2,133,762 ("'762") is only eligible for listing in respect of AstraZeneca's Notice of Compliance ("NOC") granted pursuant to New Drug Submission ("NDS") Control No. 059881, and that it is not relevant to any other submission for an NOC. The application is also for a declaration that Apotex does not need to address the '762 patent in its submission under the *Regulations*. Apotex alleges that the '762 patent is improperly listed in respect of two of AstraZeneca's three NDS's for omeprazole, as the '762 patent is not for the drug itself but for a use of the drug. Apotex also alleges that the '762 patent is not relevant to its request for an NOC as it will not be marketing omeprazole in conjunction with the new use claimed by the '762 patent.

Medicine: **Clarithromycin** (**BIAXIN**)
Applicant: Apotex Inc
Respondents: The Minster of Health and Abbott Laboratories Ltd
Date Commenced: June 5, 2002
Comment: Application for declaration that Abbott's Canadian Patent No. 2,261,732 ("'732") is ineligible for listing and is improperly listed on the Patent Register. Abbott listed the '732 patent on the Patent Register in respect of a Notice of Compliance ("NOC") that was issued on July 30, 1998. Apotex alleges that the original NOC under which Abbott began marketing Biaxin in 1992 must have been issued prior to 1993. Apotex further alleges that the Biaxin products marketed in respect of each of Abbott's NOC's have the same Drug Identification Number, and are therefore the same, and that the '732 patent is improperly listed because it is ineligible for listing under the earlier NOC.

Medicine: **Paroxetine hydrochloride anhydrate** (**PAXIL**)
Applicants: GlaxoSmithKline Inc and SmithKline Beecham PLC
Respondents: Apotex Inc and The Minister of Health
Date Commenced: June 6, 2002
Comment: Application for order prohibiting the Minister from issuing a Notice of Compliance to Apotex in respect of paroxetine hydrochloride until after the expiry of Canadian Patent Nos. 2,168,829; 2,210,023 and 2,211,522. Apotex alleges invalidity and non-infringement for all three patents. The Applicants allege that Apotex will infringe the listed patents, and that the claims of invalidity are not justified.

Medicine: **Ciprofloxacin hydrochloride** (**CIPRO**)
Applicants: Bayer AG and Bayer Inc
Respondents: Apotex Inc and The Minister of Health
Date Commenced: June 7, 2002
Comment: Application for order prohibiting the Minister from issuing a Notice of Compliance to Apotex in respect of ciprofloxacin hydrochloride until after the expiry of Canadian Patent No. 1,218,067. The application also requests a declaration that Apotex' Notice of Allegation ("NOA") is not valid as it does not comply with the *Regulations*, and that the Minister is prohibited from responding to the NOA by reason of abuse of process. Apotex has sent seven previous NOA's in respect of ciprofloxacin. Bayer also alleges that Apotex has stockpiled ciprofloxacin in contravention of the *Patent Act*, and therefore should be estopped from bringing this summary proceeding.

Medicine: **Unidentified**
Applicant: Apotex Inc
Respondent: The Minister of Health
Date Commenced: June 14, 2002
Comment: Application for an order to quash the Minister's refusal of a first-level appeal of the issuance of a Notice of Non-Compliance ("NON") and an order to treat the NON as a Clarifax, or, alternatively, to quash the NON and direct the Minister to continue to process Apotex' New Drug Submission.

Other New Proceedings

Medicine: **Influenza virus vaccines**
Applicant: Aventis Pasteur Ltd
Respondent: Attorney General of Canada
Date Commenced: May 23, 2002
Comment: Application for an order prohibiting the Minister of Public Works and Government Services from disclosing information regarding supply contracts for the Applicant's vaccines from 2001 to the present.

Medicine: **APO-MEDROXY**
Applicant: Apotex Inc
Respondent: The Minister of Health
Date Commenced: June 4, 2002
Comment: Application for an order requiring the Minister to completely consider all of the grounds of Apotex' first-level appeal of the issuance of a Notice of Non-Compliance for Apo-Medroxy 10 mg tablets. Apotex also requests an order stating that if the Minister, after consideration, refuses the appeal, the Minister will be required to provide reasons and to expedite Apotex' second-level appeal. Apotex alleges that the Minister failed to consider each of the grounds of appeal put forward in the first-level appeal, and that the Minister has not properly disposed of the appeal within the time period required by the *Management of Drug Submissions Policy*.

Medicine: **Pyrazolopyrimidinone compounds**
Plaintiffs: Bayer AG and Bayer Inc
Defendant: Pfizer Research and Development Co
Date Commenced: June 5, 2002
Comment: Action for a declaration of invalidity of claims 1 to 27 of Canadian Patent No. 2,163,446 ("'446") or, alternatively, a declaration limiting claims 25 to 27 of the '446 patent to those compounds defined as Formula (I) in the patent. Bayer alleges that claims 1 to 27 were anticipated and obvious, the specification does not fully describe the invention as set out in those claims and the claims are overly broad. Bayer alleges that claims 25 to 27 are worded so as to claim the use of compounds that fall within the general class of compounds known as cGMP PDE inhibitors, and are thus not properly limited to the pyrazolopyrimidinone compounds defined within the patent.

New Ontario Court Proceedings

Compound: **Phenylopropanolamine**
Plaintiff: Carolyn McColl
Defendants: Wyeth (formerly known as American Home Products Corp), Wyeth Ayerst Canada Inc (c.o.b. Wyeth Pharmaceuticals) and Whitehall-Robins Inc Canada (c.o.b. Wyeth Consumer Healthcare)
Date Commenced: April 2, 2002
Comment: Action under the *Class Proceedings Act, 1992* for general damages and for an order for the defendants to refund revenue received from the sale of products containing phenylopropanolamine ("PPA") and requiring the defendants to notify consumers not to ingest products containing PPA, to establish a fund for a PPA-related medical research, education and notification program, and rescinding all contracts pertaining to the purchase and sale of the defendants' products containing PPA. The plaintiff alleges that the defendants failed to properly warn consumers about various alleged side effects associated with PPA.

Medicine:	**Tamoxifen citrate** (**APO-TAMOX**)
Applicant:	Apotex Inc
Respondent:	Genpharm Inc
Date Commenced:	May 7, 2002
Comment:	Application for an interim and interlocutory order compelling Genpharm to supply Apotex with tamoxifen citrate tablets under a supply contract between the parties and for an order commencing arbitration and appointing an arbitration tribunal in respect of the dispute. Apotex alleges that Genpharm failed to supply Apotex with tamoxifen tablets on a timely basis as it was required to do under the supply agreement, resulting in inventory shortages and loss of Apotex' market share.

Medicine:	**Rofecoxib** (**VIOXX**)
Plaintiff:	William Arseneau
Defendant:	Merck Frosst Canada Inc
Date Commenced:	May 17, 2002
Comment:	Notice of Action under the *Class Proceedings Act, 1992* for negligence, claiming general and special damages alleged to have been sustained from a heart attack suffered while taking Vioxx.

Compound:	**Ethyl maltol** (**VELTOL-PLUS, ETHYL PYROMALTOL**) and **methyl maltol** (**VELTOL, PYROMALTOL**)
Plaintiff:	Newly Weds Foods Co
Defendants:	Pfizer Inc, Pfizer Canada Inc and Otsuka Chemical Co Ltd
Date Commenced:	June 10, 2002
Comment:	Action under the *Class Proceedings Act, 1992* for conspiracy, intentional interference with economic relations and anti-competitive conduct in contravention of Part VI of the *Competition Act*. The plaintiff alleges that the defendants agreed to divide sales territories and to set prices in respect of the maltol market in Canada.

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