Federal Court of Appeal | Cour d'appel fédérale

Date: 20101125

Dockets: A-129-09
A-135-09
A-139-09

Citation: 2010 FCA 320

CORAM: **NOËL J.A.**
PELLETIER J.A.
TRUDEL J.A.

Docket: A-129-09

BETWEEN:

APOTEX INC.

Appellant

and

LUNDBECK CANADA INC.

Respondent

and

THE MINISTER OF HEALTH

Respondent

and

H. LUNDBECK A/S

Respondent

Docket: A-135-09

BETWEEN:

MYLAN PHARMACEUTICALS ULC
(formerly Genpharm ULC)

Appellant

and

LUNDBECK CANADA INC.

Respondent

and

THE MINISTER OF HEALTH

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and

H. LUNDBECK A/S

Respondent

Docket: A-139-09

BETWEEN:

COBALT PHARMACEUTICALS INC.

Appellant

and

LUNDBECK CANADA INC., H. LUNDBECK A/S
and THE MINISTER OF HEALTH

Respondents

Heard at Ottawa, Ontario, on September 14, 2010.

Judgment delivered at Ottawa, Ontario, on November 25, 2010.

REASONS FOR JUDGMENT BY: NOËL J.A.

CONCURRED IN BY: PELLETIER J.A.
TRUDEL J.A.

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REASONS FOR JUDGMENT

NOËL J.A.

[1] These are three appeals from judgments rendered by Harrington J. of the Federal Court (the Applications Judge) granting the applications brought by Lundbeck Canada Inc. (the respondent or Lundbeck) to prohibit the Minister of Health (the Minister) from issuing a Notice of Compliance (NOC) to Apotex Inc. (Apotex), Mylan Pharmaceuticals ULC, formerly Genpharm ULC (Genpharm) and Cobalt Pharmaceuticals Inc. (Cobalt) (collectively the appellants) pursuant to section 6 of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, in respect of each of the appellants' generic version of the drug containing escitalopram for use as an antidepressant, until after the expiration of Canadian Patent No. 1,339,452 (the '452 patent).

[2] The applications before the Federal Court were heard consecutively over a three-week period from December 1 to December 18, 2008. Although they were never joined, the Applications Judge opted to dispose of the applications on the basis of a single set of reasons. The following reasons dispose of the three appeals.

[3] The issue in the three appeals is whether the Applications Judge properly held that the appellants' respective allegations of invalidity regarding the '452 patent were not justified and that accordingly they had failed to show that their generic version of escitalopram would not infringe this patent. For the reasons which follow, I am of the view that the appeals should be dismissed.

BACKGROUND

[4] Apotex, Genpharm and Cobalt filed Notice of Allegations (NOAs) on April 20, January 23 and June 18, 2007 respectively, making a number of allegations, some common and some specific to the particular applicant. At the core of each NOA is the allegation that the '452 patent is an invalid selection patent and that the alleged invention was both obvious and anticipated. Also raised are allegations that the '452 patent lacks utility, fails to soundly predict the invention (Apotex), provides insufficient disclosures (Apotex, Genpharm and Cobalt) and is ambiguous (Apotex and Genpharm).

[5] The '452 patent, entitled "Enantiomers of Citalopram and Derivatives Thereof", was applied for in June 1989 by the respondent, based on a United Kingdom priority date of June 1988. The patent was granted in 1997 and expires in 2014. It claims escitalopram as a useful antidepressant and describes two methods of obtaining it.

[6] The claims at issue are claims 1 and 3, as well as claim 5, insofar as it is dependent on claim 3:

> - 1 -
> A compound selected from substantially pure (+)-1-(3-Dimethylaminopropyl)-1-(4'-fluorophenyl)-1, 3-dihydroisoben-zofuran-5-carbonitrile and non-toxic acid addition salts thereof.
>
> […]
>
> - 3 -
> A pharmaceutical composition in unit dosage form useful as an antidepressant comprising a pharmaceutically-acceptable diluent or adjuvant and, as an active ingredient, an effective amount of a compound as defined in [c]laim 1.

[…]

- 5 -

A pharmaceutical composition in unit dosage form, useful as an antidepressant according to claim 3 or 4, wherein the active ingredient is present in an amount from 0.1 to 100 milligram per unit dose.

[7] It is also useful to set out claim 2:

A compound of [c]laim 1 being the pamoic acid salt of (+)-1-(3-dimethylaminopropyl)-1-(4'-fluorophenyl-1, 3-dihydroisobenzofuran-5-carbonitrile.

[8] The '452 patent notes that citalopram was disclosed in the now expired U.S. patent number 4,136,193 (U.S. patent '193). U.S. patent '193 disclosed a formula which might produce a few hundred compounds and specifically claimed citalopram as a useful antidepressant.

[9] The '452 patent also indicates that a precursor of citalopram, a diol, was disclosed in U.S. patent number 4,650,884 (U.S. patent '884), filed in August 1985 and entitled "Novel Intermediate and Methods for Its Preparation".

[10] The Applications Judge provided a useful summary of the relevant chemistry with which the parties do not take issue (Reasons, paras. 22 to 28). It can be seen from this summary that the chemical compound at issue in this case, escitalopram, is one of the two enantiomers of citalopram, a racemate. Escitalopram is also known as (+) citalopram and S-citalopram.

[11] Carbon-centered molecules, like the compound at issue, have a three-dimensional structure. If that carbon atom is bonded to four different atoms or groups of atoms, as is the case here, the molecule is described as having an asymmetric centre. These chemical compounds are identical save that they exist in two space-occupying forms called "enantiomers," which are non-superimposable mirror images of one another. Such asymmetric molecules are called chiral, coming from the Greek word for hand, as a left hand and a right hand are mirror images of each other but are not superimposable. When a molecule with these characteristics is synthesized, both enantiomers are produced in equal proportions. This mixture is called a racemate or a racemic mixture.

[12] When a drug is a racemate, although the two enantiomers of the drug have the same molecular formula, they can interact differently within the human body. Just like the key and lock analogy, the racemate and each of its enantiomers can dock in different ways with biomolecules in the body; the consequence being that they can have pharmacological properties of their own.

[13] Because of their identical chemical formula, two unrelated nomenclatures are used to identify enantiomers. The first nomenclature is based on the direction in which the enantiomer directs the plane of polarized light. If the plane is turned clockwise, the enantiomer is identified as (+), d or dextro-rotary; if the plane is turned counter-clockwise, it is identified as (-), l or levo-rotary. Escitalopram is the (+) enantiomer of citalopram: it thus directs the plane of light in a clockwise direction. Because a racemate is a mixture of two enantiomers that rotate polarized light in opposite directions, it is designated as (+/-).

[14] The second nomenclature is the Cahn-Ingold-Prelog convention which specifies absolute configuration. The substituents around the chiral centre are "sized" according to their atomic numbers. If the sequence from the largest to the smallest flows in a clockwise direction, the enantiomer is assigned the R or *rectus* designation. Otherwise it is assigned the S or *sinister* designation. A racemate is designated (R, S). Escitalopram is the S-enantiomer of citalopram.

[15] The above summary is drawn from the expert evidence of Professor Davies who was called by Lundbeck in the three proceedings and Dr. Newton who was called by both Genpharm and Cobalt in their respective proceedings (Reasons, para. 28). Seven other experts were called: Professor Clark testified on behalf of Lundbeck in all three proceedings; Dr. Keana, Dr. McClelland and Professor Ward appeared on behalf of Apotex; Professor Chong and Dr. Collicott on behalf of Genpharm; and Dr. Kissinger on behalf of Cobalt.

[16] Each expert advanced views on racemates, the methods to resolve them and the degree of difficulty which this can present (Reasons, paras. 63 to 72). In the end, the Applications Judge came to the view that the opinions of Professors Davies and Clark who testified on behalf of Lundbeck in all three proceedings were to be preferred.

RELEVANT LEGAL PROVISIONS

[17] Given the date on which the '452 patent was applied for, the *Patent Act*, R.S.C. 1985, c. P-4 (the *Patent Act*) as it read prior to October 1, 1989, applies. The term "invention" is defined in section 2 as follows:

[…] any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter;	Toute réalisation, tout procédé, toute machine, fabrication ou composition de matières, ainsi que tout perfectionnement de l'un d'eux, présentant le caractère de la nouveauté et de l'utilité.

[18] Subsection 27(1) regarding disclosure reads:

Subject to this section, any inventor or legal representative of an inventor of an invention that was *(a)* not known or used by any other person before he invented it, *(b)* not described in any patent or in any publication printed in Canada or in any other country more than two years before presentation of the petition hereunder mentioned, and *(c)* not in public use or on sale in Canada for more than two years prior to his application in Canada, may, on presentation to the Commissioner of a petition setting out the facts, in this Act termed the filing of the application, and on compliance with all other requirements of this Act, obtain a patent granting to him an exclusive property in the invention.	Sous réserve des autres dispositions du présent article, l'auteur de toute invention ou le représentant légal de l'auteur d'une invention peut, sur présentation au commissaire d'une compétition exposant les faits, appelée dans la présente loi le « dépôt de la demande », et en se conformant à toutes les autres prescriptions de la présente loi, obtenir un brevet qui lui accorde l'exclusive propriété d'une invention qui n'était pas : *a)* connue ou utilisée par une autre personne avant que lui-même l'ait faite; *b)* décrite dans un brevet ou dans une publication imprimée au Canada ou dans tout autre pays plus de deux ans avant la présentation de la pétition ci-après mentionnée; *c)* en usage public ou en vente au Canada plus de deux ans avant le dépôt de sa demande au Canada.

[19] Subsection 34(1) concerning the specification reads as follows:

An application shall in the specification of the invention	Dans le mémoire descriptif, le demandeur :

(a) correctly and fully describe the invention and its operation or use as contemplated by the inventor;	*a)* décrit d'une façon exacte et complète l'invention et son application ou exploitation, telles que les a conçues l'inventeur;
(b) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is mostly closely connected, to make, construct, compound or use it;	*b)* expose clairement les diverses phases d'un procédé, ou le mode de construction, de confection, de composition ou d'utilisation d'une machine, d'un objet manufacturé ou d'un composé de matières, dans des termes complets, clairs, concis et exacts qui permettent à toute personne versée dans l'art ou la science dont relève l'invention, ou dans l'art ou la science qui s'en rapproche le plus, de confectionner, construire, composer ou utiliser l'objet de l'invention;
…	…

THE FEDERAL COURT DECISION

[20] Although seized with distinct applications, the Applications Judge opted to issue one set of reasons. He explained that counsel for the appellants were invited to attend all three hearings, that memoranda of fact and law in all three applications were exchanged and that the commonality of the applications greatly surpassed their distinctiveness (Reasons, para. 20). He added that the relevant distinctions would be made in the course of his reasons (Reasons, para. 21).

[21] The Applications Judge noted at the beginning of his analysis that patent construction was at the heart of the dispute and outlined the applicable principles as set out by the Supreme Court in

Free World Trust v. Électro Santé Inc., 2000 SCC 66, [2000] 2 S.C.R. 1024 [*Free World Trust*] and *Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, [2000] 2 S.C.R. 1067.

[22] According to the Applications Judge, the invention disclosed in the '452 patent relates to the two novel enantiomers of citalopram including their pharmaceutically acceptable salts and their use as an antidepressant. The '452 patent also notes that previous attempts at resolving citalopram, which the patent states were disclosed in the U.S. patent '193, had failed and that it was discovered that a precursor of citalopram, a diol disclosed in U.S. patent '884, could be resolved into its enantiomers and then converted to the enantiomers of citalopram in a stereoselective way. The '452 patent describes two methods to obtain escitalopram (Reasons, para. 41).

[23] With respect to the selection patent issue, the question was whether escitalopram had a special or unexpected advantage over citalopram (Reasons, para. 37). The Applications Judge found that escitalopram was at best 1.6 times more potent than citalopram. This was not sufficiently unexpected to serve as the foundation for a selection patent "[s]ince it was well within the realm of possibility that more, and indeed sometimes all, of the desired biological activity of a racemate might rest within one enantiomer rather than in the other" (Reasons, para. 43). He thus concluded that if the '452 patent was a selection patent, it was invalid.

[24] However, the Applications Judge held that the '452 patent was not a selection patent. He found instead that it was a patent for a new substance: substantially pure escitalopram. He reached that conclusion based on the fact that this particular compound was not disclosed let alone claimed

in either U.S. patents ‘193 or ‘884 (Reasons, para. 42). In coming to this conclusion, the Applications Judge dismissed the argument that a patent for a racemate automatically discloses and claims the two enantiomers (Reasons, para. 47).

[25] With respect to anticipation, the Applications Judge after reviewing the evidence held that the documents put into evidence by the appellants including the prior patents did not disclose escitalopram as a useful antidepressant and could not therefore form the basis for an allegation of anticipation by prior disclosure. Although it was known to the skilled addressee that within citalopram were two enantiomers, and that it might not be a surprise that one might be more potent than the other, one would not know the qualities of the two enantiomers without separating and testing them (Reasons, paras. 50 to 52).

[26] Turning to obviousness, the Applications Judge applied the four-step approach identified by the Supreme Court in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, [2008] 3 S.C.R. 265 [*Sanofi*]. First, he found that the skilled addressee was a “team centered around a medicinal chemist who had access to and makes use of others with different skill sets such as analytical chemists and psychiatrists” and that “theoretical knowledge of, and practical experience in, the methods of resolving racemate were essential” (Reasons, paras. 36 and 53 to 58).

[27] Dealing with the second step, the Applications Judge found that the construction of the relevant claims posed no difficulty, *i.e.* claim 1 was for substantially pure escitalopram and non-toxic additional salts thereof, claim 3 was for a chemical composition in unit dosage form useful as

an antidepressant, and claim 5 was for a unit dosage form wherein the active ingredient ranged from 0.1 to 100 milligrams per unit dose. He noted that the ‘452 patent did not claim that escitalopram was better than citalopram (Reasons, para. 59).

[28] As to the difference between the prior art and the inventive concept underlying the ‘452 patent, the Applications Judge found that the prior art disclosed citalopram to be useful as an antidepressant, but that it neither disclosed its two enantiomers nor predicted that either would be useful as an antidepressant. He held that the inventive step was the resolution of citalopram in sufficient quantity to permit the testing disclosed in the patent; without it, it was impossible to determine the usefulness of the enantiomers (Reasons, para. 60).

[29] Turning to the fourth step – *i.e.* whether the claimed invention was obvious to the skilled addressee – the Applications Judge after reviewing the expert testimony considered the methods for resolving citalopram available in 1988, the route taken by Lundbeck to resolve citalopram and the allegation that the prior art disclosed the resolution of citalopram (Reasons, paras. 63 to 74). He first noted that motivation is not instructive in this case (Reasons, paras. 79 to 83). Concerning the resolution of citalopram, or of its precursor (the diol which is a racemate), the Applications Judge described the two methods available to resolve citalopram at the claim date: the classical method of fractional crystallization and chiral high pressure liquid chromatography (HPLC) (Reasons, paras. 84 to 88). The Applications Judge later referred to Lundbeck’s eight-year quest to resolve citalopram (Reasons, paras. 90 to 102). He found that it was not obvious to try to resolve citalopram

and that in any event, it was certainly not obvious that what was being tried would work (Reasons, para. 103).

[30] The Applications Judge went on to hold that an inventive step was required to resolve citalopram with the result that the allegation of obviousness was not made out (Reasons, para. 124).

[31] The Applications Judge then addressed Genpharm's contention that escitalopram was anticipated on the theory that the body resolves citalopram by itself into the two enantiomers. According to Genpharm, the instruction to ingest citalopram in U.S. patents '193 and '884 results in the production of escitalopram in the body. Genpharm made this proposition on the basis of the decision of the House of Lords in *Merrell Dow Pharmaceuticals Inc. v. HN Norton and Co. Ltd.*, [1995] UKHL 14, [1996] RPC 76 [*Merrell Dow*] (Reasons, paras. 125 to 128).

[32] The Applications Judge distinguished *Merrell Dow* and held that Genpharm's contention that the body resolves citalopram into substantially pure escitalopram was based on conjecture (Reasons, para. 129).

[33] The Applications Judge then dealt with Genpharm's allegation that claim 1 was ambiguous because it did not define what it meant by "substantially pure escitalopram". The Applications Judge found no ambiguity since the examples given showed purity in excess of 99%; one expert asserted that "substantially pure" would mean at least 95% since a standard method only detects impurities if they are present at a level of at least 5% (Reasons, para. 130). The Applications Judge

also dismissed Apotex's suggestion that the +/- nomenclature used is ambiguous because different solvents may rotate light in a different way thus altering the +/- designation. He pointed out that the solvents to be used were fully described in the patent (Reasons, para. 131).

[34] The Applications Judge also dismissed Apotex's argument that the '452 patent did not offer a sound prediction of utility because it was based on studies conducted on rodents. According to the Applications Judge the testing done on rodents, which was the same as had been done for citalopram, soundly predicted that escitalopram would be useful as an antidepressant in humans. The Applications Judge concluded that "[u]sefulness was promised, usefulness was predicted and usefulness was delivered" (Reasons, para. 134).

[35] Finally, the Applications Judge dismissed Apotex's contention that escitalopram lacked utility on the basis that the pamoic salt of escitalopram in claim 2 was toxic. Relying on *Burton Parsons Chemicals, Inc. v. Hewlett-Packard (Canada) Ltd.*, [1976] 1 S.C.R. 555, [*Burton Parsons*], he held that the skilled addressee would not use a toxic salt (Reasons, para. 139).

ALLEGED ERRORS

Issues common to all three appellants

The '452 patent is an invalid selection patent

[36] All three appellants submit that the '452 patent is an invalid selection patent. They argue that the '452 patent is a selection because escitalopram was disclosed in U.S. patent '193 which claimed citalopram and its use as an antidepressant. Although expressed in a different way, both

Apotex and Genpharm submit that the Applications Judge misapprehended and misapplied the law of selection patents by requiring a prior enabling disclosure or claim for escitalopram in order to characterize the ‘452 patent as a selection patent.

[37] The appellants submit, relying primarily on the decision of the Supreme Court in *Sanofi*, that courts have treated patents for enantiomers as selection patents even though the enantiomers were not anticipated. As well, they refer to the decision of this Court in *Pfizer Canada Inc. v. Canada (Minister of Health)*, 2008 FCA 108 [*Pfizer*] to show that patents claiming an enantiomer of a previously disclosed racemate have been held to be selection patents. The decisions of the Federal Court in *Janssen-Ortho Inc. v. Novapharm Ltd.*, 2004 FC 1631 [*Janssen-Ortho I*] and *Janssen-Ortho Inc. v. Novapharm Ltd.*, 2006 FC 1234 [*Janssen-Ortho II*] are also referred to.

[38] Genpharm for its part emphasizes the fact that the ‘452 patent describes escitalopram as a “surprising discovery”. According to Genpharm, the “surprise” is the “special quality” that would validate escitalopram as a selection from citalopram.

[39] Apotex argues that the Applications Judge erred in construing the claims contained in U.S. patent ‘193 from the perspective of a patent lawyer. By observing that it would be unwise to draft U.S. patent ‘193 so as to include untested compounds because to do so would leave the patent open to an overclaim attack, the Applications Judge took the perspective of the patent draftperson instead of the person of ordinary skill in the art and made inquiries which are not permissible when construing the patent.

[40] Apotex contends that by describing the subject matter of U.S. patent ‘193 in terms of a chemical formula without reference to optical information, the draftsperson intended to encompass all compounds having the same chemical formula: the racemate, R-citalopram and S-citalopram. It follows that U.S. patent ‘193 discloses and claims escitalopram.

Anticipation

[41] All three appellants argue that escitalopram was anticipated by U.S. patent ‘193. Apotex alleges that escitalopram is formed “always”, “inevitably” and “with no possibility of error” upon making citalopram and that the Applications Judge found as such when he noted that anyone making escitalopram would infringe on U.S. patent ‘193 (Reasons, para. 83). Genpharm also relies on this passage.

[42] Cobalt submits that the Applications Judge’s finding that U.S. patent ‘193 did not disclose the enantiomers of citalopram is inconsistent with his finding that an undergraduate student in organic chemistry would have known that citalopram was made up of two enantiomers. Since the person skilled in the art would be reading with a mind willing to understand the patent, Cobalt alleges that U.S. patents ‘193 and ‘884 disclosed and enabled both enantiomers of citalopram.

[43] Genpharm contends that escitalopram was anticipated because both U.S. patents ‘193 and ‘884 provided instruction to ingest citalopram which, if followed, would lead to the production of substantially pure escitalopram in the body. Genpharm submits that the Applications Judge erred in rejecting the evidence adduced on this point as “outright conjecture” without analyzing it.

Issues common to Genpharm and Cobalt

Obviousness

[44] With respect to obviousness, Genpharm submits that there was no difference between the state of the art and the '452 patent. In particular, Genpharm contends that since U.S. patents '193 and '884 disclosed to the person skilled in the art citalopram and its two enantiomers and, as their usefulness as an antidepressant was known, the '452 patent contributes nothing to the existing body of knowledge. In any event, it was more or less evident that what was being tried ought to work.

[45] Genpharm further alleges that the Applications Judge erred in assuming that 100 milligrams of escitalopram were required for testing. With respect to the resolution of citalopram using chiral HPLC, Genpharm submits that the Applications Judge made a palpable and overriding error in concluding that analytical columns could not have produced sufficient material for detection and for the biological testing required by the '452 patent. Genpharm also submits that it would have been obvious in 1988 to use the intermediate diol, disclosed in U.S. patent '884, to obtain substantially pure escitalopram.

[46] With respect to the Applications Judge's finding that the experts were operating with hindsight, Genpharm submits that the Applications Judge failed to distinguish between inevitable and impermissible hindsight. Genpharm further alleges that, due to the *U.S. Food and Drug Administration 1987 Guidelines* (1987 FDA Guidelines), drug companies were motivated to resolve racemates so as to obtain information on the properties of the enantiomers. Finally, Genpharm

submits that Dr. Bøgesø, the co-inventor of citalopram, had built-in biases which prevented him from quickly resolving citalopram; the person skilled in the art would not have such biases.

[47] Cobalt also submits that it was obvious for Lundbeck to resolve citalopram because citalopram and its enantiomers were known to the person skilled in the art as was their use as an antidepressant. It would therefore have been self-evident to Lundbeck to pursue escitalopram and it had a fair expectation of success.

Procedural fairness and inadequacy of reasons

[48] Genpharm and Cobalt allege that the Applications Judge erred in using evidence that was not led in their respective proceeding and in issuing one set of reasons for three different proceedings.

[49] Genpharm contends that the Applications Judge's reasons do not adequately identify the specific findings with respect to Genpharm regarding anticipation and obviousness. According to Genpharm, this makes "meaningful review impossible and prevents [it] from properly arguing its appeal" (Genpharm's memorandum of fact and law, para. 48).

[50] Cobalt further argues that since Lundbeck had access to the documents filed in all three proceedings and made submissions comparing the evidence, Lundbeck had a tactical advantage that was prejudicial to it.

Issues specific to Apotex

Sound prediction

[51] Apotex argues that the utility of escitalopram was not soundly predicted. In particular, there was "nothing in the '452 patent to correlate the ability of citalopram to cause changes in mouse motor function and rat brain-cell effects with its clinical antidepressant effect in humans" (Apotex's memorandum of fact and law, para. 68). Apotex contends that without this correlative information, there can be no factual basis for sound prediction.

[52] Apotex also contends that the '452 patent lacks utility because it covers a toxic pamoate salt which Lundbeck admitted is toxic in a 2004 patent application. Further, Apotex submits that the Applications Judge erred in construing claim 1 of the '452 patent as excluding such salt because it would be obvious to a person skilled in the art not to use toxic salt. According to Apotex, the Applications Judge's task was to determine how the person skilled in the art would interpret the words of claim 1 – "non-toxic acid addition salts" – at the date of issue of the '452 patent. Apotex submits that the Applications Judge erred in his construction of claim 1.

Ambiguity

[53] Apotex submits that the '452 patent does not teach the person skilled in the art how to use the solvents to obtain escitalopram. Since there was no such indication, it cannot be said that the patent was defined in "full, clear, concise and exact" terms (section 34 of the *Patent Act*).

Insufficiency of disclosure

[54] Finally, Apotex submits that the disclosure in the '452 patent is insufficient for laying a false trail regarding human administration of escitalopram and that the Applications Judge "erroneously understood Apotex's allegation to be made pursuant to section 53 of the *Patent Act*" rather than section 34 (Apotex's memorandum of fact and law, para. 90). Apotex contends that had the proper inquiry been made, the allegation of insufficiency would have been justified.

ANALYSIS AND DECISION

[55] Before embarking on the analysis, it is useful to recall that questions of law are to be ascertained on a standard of correctness and that factual findings cannot be reversed absent a palpable and overriding error (*Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R. 235). The identification of the legal requirements for the existence of a selection patent as well as the construction of the relevant claims in the patents considered by the Applications Judge give rise to questions of law. The remaining issues are for the most part factual.

[56] The appellants essentially reiterate on appeal the arguments which they made before the Applications Judge. The reasons which follow address most of these issues. With respect to those that are not addressed, I endorse the reasons of the Applications Judge in disposing of them.

Selection patent

[57] The selection patent issue, which is central to each of the appellants' case, presents itself in simple terms: the appellants maintain that the '452 patent is a selection patent and as the

Applications Judge found that the selected compound had no special advantage, the patent is invalid.

[58] The Applications Judge held that the '452 patent was not a selection patent because, in his view, escitalopram was an original compound which was not selected from a previously patented compound. He therefore conducted his analysis on the basis that the '452 patent was an ordinary patent for an original compound and as he found this compound to be both novel and useful (see the definition of "invention" in section 2 of the *Patent Act*), he held the patent to be valid. At the same time, he made it clear that escitalopram's claimed usefulness was no greater than citalopram's and that therefore the invention, as claimed, had no special advantage over citalopram.

[59] The question whether the '452 patent is a "selection patent" depends on the legal meaning to be given to these words. The term "selection patent" is not found in the *Patent Act*. However, the Supreme Court in *Sanofi* held that a system of genus and selection patents is acceptable in principle under the *Patent Act*, on the line of authority stemming from in ***I. G. Farbenindustrie A. G.'s Patents*** (1930), 47 R.P.C. 289 (Ch. D.) [***Farbenindustrie***]. The Supreme Court refers to that case to circumscribe what is to be considered as a selection patent (*Sanofi*, para. 9):

> The *locus classicus* describing selection patents is the decision of Maugham J. in *[Farbenindustrie]*. At p. 321, he explained that in the field of chemical patents (which would of course include pharmaceutical compounds), there are often two "sharply divided classes". The first class of patents, which he called originating patents, is based on an originating invention, namely, the discovery of a new reaction or a new compound. The second class comprises patents based on a selection of compounds from those described in general terms and claimed in the originating patent. Maugham J. cautioned that the selected compounds cannot

> have been made before, or the selection patent "would fail for want of novelty". But if the selected compound is "novel" and "possess[es] a special property of an unexpected character", the required "inventive" step would be satisfied (p. 321). At p. 322, Maugham J. stated that a selection patent "does not in its nature differ from any other patent".
>
> [My emphasis]

[60] In accepting that a system of genus and selection patents was acceptable under Canadian law, the Supreme Court explained that its application was consistent with the *Patent Act* (*Sanofi*, para. 31):

> Section 27(1) of the Act requires as a condition for obtaining a patent that the invention was not "known or used" and was not "described" in any patent or any publication more than two years before the patent application was filed. In the context of genus and selection patents, in ***E. I. Du Pont de Nemours & Co. (Witsiepe's) Application***, [1982] F.S.R. 303 (H.L.), Lord Wilberforce stated, at p. 311:
>
> > It is the absence of the discovery of the special advantages, as well as the fact of non-making, that makes it possible for such persons to make an invention related to a member of the class.
>
> The compound made for the selection patent was only soundly predicted at the time of the genus patent. It was not made and its special advantages were not known. It is for those reasons that a patent should not be denied to the inventor who made and discovered the special advantages of the selection compound for the first time.

[61] It is apparent from the foregoing that a selection patent must be preceded by a prior patent – referred to as a genus or originating patent – which, in the words of Maugham J. in *Farbenindustrie*, describes in general terms and claims compounds from which a selection is made. That the selection

is made from compounds generally described and claimed in a prior patent does not necessarily mean that the selected compound is anticipated (*Sanofi*, para. 19). So long as the selected compound is new – in that it has never been made – and has a special advantage that was not previously known and that is peculiar to it, patent protection may be available (*Sanofi*, paras. 10 and 31). However, a definitive conclusion cannot be reached absent a complete analysis (*Eli Lilly Canada Inc. v. Novopharm Limited*, 2010 FCA 197, paras. 27 to 33 [*Eli Lilly*]). In this respect, it is worth repeating that a selection patent does not differ from any other patent (*Sanofi*, para. 9).

[62] Against this background, the first question which has to be answered is whether U.S. patents '193 and '884, together or singly, describe in general terms and claim compounds from which escitalopram was selected. In this respect, the recent decision of this Court in *Eli Lilly* on which the parties made supplemental submissions is of limited assistance since it was accepted that the compound in issue in that case had been selected from a previously patented class of compounds (*Eli Lilly*, para. 7).

[63] The Applications Judge answered this question in the negative. In particular, he found that U.S. patent '193 claims citalopram and that this claim did not encompass escitalopram. Apotex made the point that escitalopram was nevertheless within the claim because the subject matter of that patent was described in terms of a chemical formula without optical information distinguishing the racemate from the enantiomers.

[64] However, the Applications Judge held that the person skilled in the art would have read the formula, as of the claim date, as referring to the compound produced by the formula, *i.e.* the racemate, and nothing else. He came to this conclusion because no stereochemical information was provided. Given this, he held that the skilled addressee would not have read U.S. patent '193 as claiming anything other than the racemate (see Professor Davies' affidavit at para. 85, A-129-09 Appeal Book, Vol. 4, p. 934; A-135-09 Appeal Book, Vol. 4, p. 1099; A-139-09 Appeal Book, Vol. 4, p. 1337).

[65] In so holding, the Applications Judge acknowledged that citalopram's chemical structure – and the chemical formula reflecting it – reveals the existence of the enantiomers. However, he rejected the argument that this in itself was sufficient to read U.S. patent '193 as claiming the enantiomers. In particular, he rejected the submission that *Sanofi* is authority for the proposition that a claim for a racemate is *ipso facto* a claim for its two enantiomers (Reasons, para. 47).

[66] I can detect no error in this regard. Contrary to what is asserted, the Supreme Court in *Sanofi* did not hold that a claim for a racemate automatically includes a claim for its enantiomers. The conclusion in *Sanofi* that the genus patent also claimed the enantiomers is based on claims 1 and 14 thereof which specifically claimed the racemate and the two enantiomers (*Sanofi*, paras. 101 and 103).

[67] The appellants made the further argument that the decision of this Court in *Pfizer* shows that a patent claiming an enantiomer of a previously disclosed racemate can be viewed as a selection

patent. No doubt that is so. However, this depends on the particularities of the patents in issue. In *Pfizer*, the patent labeled as a selection patent (the '546 patent) states that the enantiomer in question was among compounds previously claimed in the prior (*i.e.* genus) patent (*Pfizer*, para. 47). No such statement appears in the '452 patent.

[68] With respect to the decision of the Federal Court in *Janssen-Ortho II*, it is significant that Hughes J., who heard the infringement action, did not deal with the patent in issue in that case as a selection patent even though the relevant claim was for an enantiomer of a previously disclosed racemate. In so doing, he declined to follow the approach of Mosley J. in *Janssen-Ortho I* who treated the same patent as a selection patent in the context of an earlier NOC proceeding. However, Mosley J. held the patent to be a selection patent only after finding that the knowledge required to separate the two enantiomers was common to the person skilled in the art (*Janssen-Ortho I*, para. 53), a finding that was not shared by Hughes J. on the evidence in the infringement action (*Janssen-Ortho II,* para. 104).

[69] Apotex further submits that the Applications Judge erred in making the existence of a selection patent dependent on specific disclosure or claim of the selected compound in a prior patent. The decision of the Federal Court, Trial Division in *Pfizer Canada Inc. v. Apotex Inc.* (1997), 77 C.P.R. (3d) 547, page 556 is relied upon. With respect, the Applications Judge did no such thing. A selection patent, by definition, is directed at a compound which comes within those generally described and claimed in a prior patent. What the Applications Judge found is that

escitalopram did not come within such a description because it was not amongst those previously described and claimed.

[70] In construing the claims of U.S. patent '193, the Applications Judge noted that it was known at the relevant time that some enantiomers are toxic and that escitalopram's utility could not be ascertained without first resolving citalopram, which had yet to be done. After pointing out that one who overclaims stands to loose everything, he concluded that the skilled person would not have read the relevant claims as extending to the enantiomers (Reasons, para. 48):

> … If to claim a racemate useful in the treatment of depression is to claim the same usefulness for each of the two enantiomers then in such circumstances the inventor would have overclaimed and lost everything. …

[71] The only attack of significance against this reasoning is Apotex's contention that in so holding the Applications Judge did not construe the claims from the perspective of the person skilled in the art, but from that of a patent agent or lawyer concerned that it would be imprudent to claim the two enantiomers.

[72] The criticism is justified. A claim should not be construed with an eye to issues of validity or infringement. However, if one moves away from the perspective of the draftsperson concerned with issues of validity, it remains that the person skilled in the art would not read the claim as extending to compounds which were not known to have the promised utility. The Applications Judge having found as a fact that it was impossible to know at the claim date which, if either, of the two enantiomers of the racemate would be useful in treating depression, read the claim as not

extending beyond the compound which was known to achieve the promised result and which was specifically claimed for that purpose, *i.e.* the racemate. Although the appellants take issue with the finding which underlies this conclusion, it was open to the Applications Judge on the record before him (see Dr. Bøgesø's affidavit at para. 24, A-129-09 Appeal Book, Vol. 2, p. 245; A-135-09 Appeal Book, Vol. 2, p. 202; A-139-09 Appeal Book, Vol. 4, p. 1054; see also Professor Clark's affidavit, A-129-09 Appeal Book, Vol. 3, p. 513; A-135-09 Appeal Book, Vol. 3, p. 464; A-139-09 Appeal Book, Vol. 5, p. 1492).

[73] Genpharm made the further argument that the '452 patent was framed by the inventor as a selection patent and therefore should be treated as such. In this respect, Genpharm points to wording which appears under the heading "Summary of invention" as follows: "… it was shown to our surprise that almost all [the activity] resided in [escitalopram]". The Applications Judge qualified these words as "puffery" after noting that no promise is made that escitalopram is better than citalopram (Reasons, para. 59).

[74] Genpharm's argument on this point appears to be that since a selection patent must claim a particular advantage described as a "surprise", the claim to a surprising result supports the view that the patent in issue is a selection patent. However, it remains that the surprise must be in relation to an advantage over a previously patented compound.

[75] In the present case, it does not follow from the statement "… to our surprise … almost [all the activity] resided in [escitalopram]" that the compound is better than citalopram as an

antidepressant. This explains why nowhere is it asserted in the patent that escitalopram is superior to citalopram. Indeed, the evidence shows that as of the claim date and up to 1992, Dr. Bøgesø, the co-inventor, was of the view that citalopram and escitalopram were equipotent (see the article published by Dr. Bøgesø in 1992, A-135-09 Appeal Book, Vol. 24, p. 7562). In this respect, the Applications Judge twice noted in the course of his judgment that it was only post the '452 patent that escitalopram was found to be more potent than citalopram (Reasons, paras. 50 and 133). It is clear that no special advantage is claimed in express terms in the '452 patent and it is equally clear that no such claim can be inferred from the statement relied upon by Genpharm.

[76] In further support of their contention that escitalopram is a selection patent, Apotex and Genpharm seized on a passage from the reasons of the Applications Judge that appears at first blush to be at odds with his analysis as a whole. In considering the degree of motivation to come up with the invention, the Applications Judge stated (Reasons, para. 83):

> There is also evidence from Dr. Newton in the Genpharm and Cobalt applications that pharmaceutical companies were not particularly interested in resolving racemates which were covered by a patent issued to a competitor. There was no bonhomie about this. Not only would the patentee likely have a head start on resolving the racemate, but at best one would end up in cross licensing agreements. If a competitor produced escitalopram, it probably could not use it because it infringed the citalopram patent. On the other hand, Lundbeck could not use escitalopram. Research and development may well have been directed to other molecules as suggested by Professor Davies. Suffice it to say that I do not consider the evidence respecting motivation helpful in considering whether the invention of escitalopram was obvious.
>
> [Emphasis by the appellants]

[77] Apotex and Genpharm both suggest that this should be read as a finding that the ‘452 patent did infringe one or the other U.S. patents or both, which can only mean that escitalopram had been previously disclosed and claimed. In my view, such a finding would run counter to the analysis and make the reasons incoherent.

[78] While the words could have been better chosen, the Applications Judge was simply saying that competitors were not motivated to pursue the resolution of citalopram because of the concern that producing escitalopram *might* infringe the citalopram patent. When considered in the context of the reasons, the passage cannot be read otherwise.

[79] In my view therefore, the Applications Judge correctly held that the ‘452 patent is an ordinary patent for an original compound and that its validity was to be assessed on that basis.

Anticipation

[80] Apotex and Cobalt submit that the ‘452 patent is anticipated by the prior art, in particular by the two U.S. patents. For its part, Genpharm submits, relying on the English case *Merrell Dow*, that the ‘452 patent is anticipated because the instructions to ingest citalopram in U.S. patents ‘193 and ‘884 provided directions which, if followed, resulted in the production of substantially pure escitalopram in the body.

[81] The test for anticipation was re-stated in *Sanofi* where Rothstein J. noted that an invention is anticipated – *i.e.* lacks novelty – when it is disclosed and enabled. Referring to the reasons of Lord

Hoffman in *Synthon B.V. v. SmithKline Beecham plc*, [2006] 1 All ER 685, [2005] UKHL 59, Rothstein J. stated that disclosure "means that the prior patent must disclose [the] subject matter, which, if performed, would necessarily result in infringement of that patent …" (*Sanofi*, para. 25). At the disclosure stage, the person skilled in the art "is simply reading the prior patent for the purposes of understanding it" and there is no trial and error (*Sanofi*, para. 25). Enablement "means that the person skilled in the art would have been able to perform the invention" (*Sanofi*, para. 26). Enablement needs to be considered only if the invention is found to be disclosed. Trial and error is permitted at this stage (*Sanofi*, para. 27).

[82] The Applications Judge followed this approach. He held that escitalopram was not disclosed (and therefore not anticipated) by the two U.S. patents. He came to this conclusion because "if the subject matter of either prior U.S. patent were worked, the result would be a racemate, not an enantiomer" (Reasons, para. 46). I can detect no error in this regard. Otherwise, the Applications Judge correctly dismissed the contention that U.S. patents '193 and '884 automatically claimed the two enantiomers (see para. 66 above).

[83] Turning to Genpharm's allegation of anticipation, the submission is that the ingestion of citalopram results in the production by the body of substantially pure escitalopram. Relying on the reasoning in *Merrell Dow*, Genpharm maintains that this shows that escitalopram was anticipated, and contends that the Applications Judge erred in dismissing its evidence as "outright conjecture". According to Genpharm, the Applications Judge had a duty to analyze this evidence and erred in not doing so. Specifically, he failed to appreciate the difference between a conclusion based on

conjecture because it is unsupported by the evidence, and a rational conclusion based on evidence (*R. v. Hehn*, 2008 BCCA 170, paras. 20 and 26).

[84] It is not necessary to dwell on this issue or on Lundbeck's submissions challenging the application of the *Merrell Dow* decision on the facts of this case because in any event, the Applications Judge found, after considering the evidence, that the human body only produces partially resolved citalopram (Reasons, para. 129). In so holding, he relied on two articles written in 1995 which indicate that a chiral HPLC column had to be used after the extraction of blood samples to resolve citalopram (see Professor Davies' affidavit, paras. 103 to 106, A-135-09 Vol. 4, pp. 1103 and 1104; see also Rochat articles, A-135-09 Vol. 21, pp. 6525 to 6538). The finding that the human body does not produce substantially pure escitalopram was open to the Applications Judge on the evidence before him.

Obviousness

[85] Both Genpharm and Cobalt challenge the Applications Judge's conclusion that escitalopram is not obvious. Although Apotex did not take issue with this aspect of the decision in its memorandum of fact and law, counsel for Apotex made supporting arguments during the hearing.

[86] In *Sanofi*, Rothstein J. laid out the approach for obviousness as developed in the English cases *Windsurfing International Inc. v. Tabur Marine (Great Britain) Ltd.*, [1985] R.P.C. 59 (C.A) and *Pozzoli SPA v. BDMO SA*, [2007] F.S.R. 37, [2007] EWCA Civ 588 (*Sanofi*, para. 67):

> (1) (a) Identify the notional "person skilled in the art";
> (b) Identify the relevant common general knowledge of that person;
>
> (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
>
> (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[87] Rothstein J. added that an "obvious to try" test might be appropriate in "areas of endeavour where advances are often won by experimentation", such as in the pharmaceutical industry (*Sanofi*, para. 68). He listed a number of non-exhaustive factors to be applied in "accordance with the evidence of each case" (*Sanofi*, para. 69):

> 1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?
>
> 2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?
>
> 3. Is there a motive provided in the prior art to find the solution the patent addresses?

In addition the "actual course of conduct which culminated in the making of the invention" may be considered (*Sanofi*, para. 70).

[88] The Applications Judge followed this approach and found that substantially pure escitalopram was not obvious.

[89] First, the Applications Judge determined that the person skilled in the art was "a team centred around a medicinal chemist who has access to and makes use of others with different skill sets such as analytical chemists and psychiatrists" and that "[t]heoretical knowledge of, and practical experience in, the methods of resolving racemates is essential" (Reasons, paras. 36 and 58). Although the Applications Judge did not explicitly identify the common general knowledge possessed by this team, it is not in dispute that such knowledge encompassed the underlying principles of chemistry applicable to the subject matter of the '452 patent, including chirality, enantiomers, stereoisomers, racemates and optical activity, and knowledge of, and experience with, methods of resolving racemates.

[90] Second, the Applications Judge identified the invention as being substantially pure escitalopram and non-toxic additional salts thereof, as stated in claim 1 of the '452 patent. He also concluded that claims 3 and 5 were easily understood. In this respect, Genpharm and Cobalt took the position that the Applications Judge identified the invention as being "the resolution of the racemate in sufficient quantity to permit the testing disclosed in the patent" (Reasons, para. 60). With respect, this is inaccurate. A fair reading of the relevant passage shows that the Applications Judge found the invention to be substantially pure escitalopram and its useful therapeutic effect. The inventive step was the resolution of citalopram since this is what allowed for the making of this compound and the identification of its properties.

[91] Third, the Applications Judge identified the difference between the state of the art and the invention. He found that while the prior art disclosed that the racemate – citalopram – was useful as an antidepressant, it did not disclose or enable its enantiomers or even predict whether either of them would be useful as an antidepressant (Reasons, para. 60). In particular, the prior art did not teach how to resolve citalopram in order to obtain substantially pure escitalopram.

[92] Fourth, the Applications Judge applied the factors outlined in *Sanofi* for the "obvious to try" test and found that the difference between the inventive concept and the state of the art did not constitute steps that would have been obvious to the person skilled in the art. In applying this test, the Applications Judge found motivation not to be instructive (Reasons, para. 79).

[93] Genpharm and Cobalt take issue with this last conclusion. Genpharm for its part, points to the 1987 FDA Guidelines which made it clear that information concerning properties of enantiomers could be required before marketing approval was granted for the racemate. This, according to Genpharm, was compelling evidence of motivation and the Applications Judge erred in dismissing it.

[94] The existence and extent of the motivation to come up with an invention is one of fact. The Applications Judge observed that the evidence relating to the 1987 FDA Guidelines was thin and that no regulatory body had made it a requirement that details of the enantiomers be disclosed (Reasons, para. 79). As such, he refused to attribute to the 1987 FDA Guidelines the effect which Genpharm contends it should have. I can detect no error in this regard.

[95] Cobalt also criticizes the Applications Judge for failing to take into account his finding that the respondent had downplayed its interest in resolving citalopram. The Applications Judge says so much at paragraph 82 of his reasons. However, the Applications Judge did not discard motivation as a factor; he simply held that this was not "helpful" in this case (Reasons, para. 83).

[96] Genpharm on the other hand takes issue with the Applications Judge's finding as to the extent of the effort required to resolve citalopram and his conclusion that the use of chiral HPLC and the resolution of the diol were not obvious steps. With respect to the effort required to resolve citalopram, Genpharm submits that the Applications Judge erred in conducting his analysis on the basis that 100 milligrams were required for testing. According to Genpharm, 1.25 milligram was sufficient. In my view, it was open to the Applications Judge to find that 100 milligrams were necessary for testing (see Dr. Newton's cross-examination and the report referred to therein, A-135-09 Appeal Book, Vol. 29, pp. 9465 and 9569).

[97] With respect to the available methods of resolution, Genpharm contends that the evidence establishes that the skilled person would have decided to pursue chiral HPLC with a reasonable expectation that it would work and would have selected columns that would generate sufficient material to perform the biological testing required by the '452 patent. In this respect, Genpharm submits that the evidence clearly shows that analytical columns could have produced the required material testing. Indeed, it contends that the Chiralcel OD and the β-Cyclobond columns were available prior to the relevant date and subsequently were used to resolve citalopram. The issue is

again whether the Applications Judge could, on the evidence, conclude that the use of chiral HPLC was not obvious.

[98] The Applications Judge found that "[a]n analytical column will allow one to analyze which compounds and impurities are present in a given reaction mixture but, unlike a preparative HPLC, cannot be used to obtain much of the desired compound" (Reasons, para. 100 [my emphasis]). In other words, analytical columns, such as the ones referred to by Genpharm, would not have produced enough material for the testing required by the '452 patent. The Applications Judge further noted that even if the expert called by Genpharm stated that he could have resolved citalopram at the relevant time, "[t]he fact of the matter is that not one of the [the experts] had ever attempted to resolve citalopram, and it is now a fairly straightforward task" (Reasons, para. 106). In my view, it was open to the Applications Judge to find that the use of chiral HPLC was not obvious.

[99] Genpharm further contends that the Applications Judge erred in finding that the resolution of citalopram using the diol was not obvious and that there was no basis for using Mosher's acid. Genpharm submits that using the diol, which was disclosed in U.S. patent '884, was a logical starting point and that one of its experts had used Mosher's acid as a reagent at the relevant time.

[100] As to the use of the diol, the Applications Judge said (para. 103):

> … In fractional crystallization, the logical starting point was citalopram itself. If that failed, one might then try to resolve other molecules such as the diol. The experts retained by the respondents did not sufficiently divorce themselves from the knowledge they had of the alleged invention as claimed. Why select the diol disclosed in the '884 patent rather than the five precursors disclosed in the '183

> patent (sic)? Without going into the chemistry, which was intensely debated, the closure of the diol ring and its timing was a crucial process which led to discussions of SN1 and SN2 reactions. Furthermore, there was an almost infinite combination of reagents and conditions to draw from.

[101] As to the use of Mosher's acid, the Applications Judge found that there was no basis for believing that as part of routine testing, the acid in question would play a major role in the ring closure reaction. This was not part of the common general knowledge or of the prior art (Reasons, para. 110). In my view, the conclusion reached by the Applications Judge both as to the use of the diol and Mosher's acid was open to him on the evidence.

[102] Finally, Genpharm contends that the rejection of its experts because they used a measure of hindsight in expressing their opinions was also made in error. The decision of this Court in *Apotex Inc. v. Bayer AG*, 2007 FCA 243, paragraph 25 is relied upon. However, what the Applications Judge found is that reliance had been placed by these experts on knowledge that was not available at the claim date (Reasons, paras. 106 to 111). I can detect no error in this regard.

[103] It has not been shown that the Applications Judge erred in holding that the escitalopram was not obvious.

Utility

[104] Apotex takes issue with the Applications Judge's rejection of the allegation that the '452 patent lacked utility because it covers the pamoic acid salt of escitalopram which has since been

found to be toxic. The argument arises from a patent application made by the respondent in Denmark in 2004 in which it is said that the U.S. patent equivalent to the '452 patent:

> … describes the free base of escitalopram as an oil, the oxalic acid salt, pamoic salt and L-(+)-tartaric acid addition salt of escitalopram. Due to the toxicity of pamoic acid addition salts they are not suitable in pharmaceuticals.
>
> [My emphasis]

[105] In the absence of any explanation on the part of the respondent (none of which was given), this statement amounts to an admission that the pamoic acid salt of escitalopram is toxic to the point that it is not suitable in pharmaceuticals. The Applications Judge conducted his analysis on this basis. However, relying on *Burton Parsons*, he refused to invalidate the '452 patent on that ground because, in his view, the skilled person would have avoided using such a salt (Reasons, paras. 139 and 140).

[106] There is no doubt that if the pamoic acid salt of escitalopram cannot be used in pharmaceuticals, claim 2 of the '452 patent fails for lack of utility since that is precisely what it claims (claim 2 is reproduced at paragraph 7 of these reasons). I agree with Apotex that the question which had to be addressed is whether the pamoic acid salt also came within claim 1 when construed from the perspective of the skilled addressee in which case claim 1 would also fail. The Applications Judge answered this question in the negative (Reasons, para. 139).

[107] According to Apotex there is no reason to exclude the pamoic acid salt from the ambit of claim 1 since, as of the claim date, there was no suggestion that pamoate salt was toxic. Beyond this,

Apotex argues that the inventor necessarily envisaged that claim 1 would comprise the pamoic acid salt since it is listed as being within the preferred "non-toxic addition salts". Furthermore, excluding pamoate salt from the ambit of claim 1 would render claim 2, which is dependent on claim 1, meaningless.

[108] Claim 1 when looked upon on its own is clear and unambiguous: it claims substantially pure escitalopram and non-toxic acid addition salts thereof. A claim that can only be read one way cannot be altered by reference to the disclosure or the specifications. The person skilled in the art aware that some acid addition salts are toxic and that others are not, would read claim 1 for what it says, *i.e.* a claim for substantially pure escitalopram and the addition salts thereof that are "non-toxic" [my emphasis]. As the pamoic acid salt of escitalopram is toxic, it is excluded from the ambit of claim 1.

[109] Apotex nevertheless argues, relying on *Halford v. Seed Hawk Inc.*, 2004 FC 88, (2004) 31 C.P.R. (4th) 434 at paragraphs 90 to 96 (rev'd on appeal but not on this point) [*Halford*], that claim 1, being the claim on which claim 2 depends, must be given a meaning which is consistent with claim 2.

[110] The exact proposition for which *Halford* stands is that an independent claim cannot be given a meaning which renders a dependent claim redundant (*Halford*, para. 98). Reading claim 1 as including a claim for the pamoic acid salt, as Apotex suggests, would render claim 2 redundant. Claim 1 must be read for what it says. The evidence shows that the inventor was wrong about the

properties of pamoic acid salt with the result that claim 2 is a self-inflicted wound of the type described in *Free World Trust* (para.51). This does not detract from the clear and unambiguous meaning of claim 1.

[111] It has not been shown that the Applications Judge erred in rejecting Apotex's allegation that claim 1 fails for lack of utility based on the toxicity of pamoic acid salts.

[112] Apotex further submits that the utility of escitalopram was not soundly predicted by the '452 patent. In this respect, Apotex argues that there was nothing in the '452 patent to correlate the effect of citalopram on rodents and its effect on humans.

[113] As noted by the Applications Judge, a sound prediction is dependent upon a factual basis. The inventor must have an articulate and sound line of reasoning from which the promised result can be inferred from that factual basis and there must be proper disclosure (see *Apotex Inc. v. Wellcome Foundation Ltd.*, 2002 SCC 77, [2002] 4 S.C.R. 453).

[114] Using this approach, the Applications Judge noted that the test conducted on rodents was the same as that which had been conducted with respect to citalopram. Since citalopram proved to be a useful antidepressant when ingested by humans, it followed that the prediction with respect to escitalopram was sound (Reasons, para. 133).

[115] I can detect no error in this reasoning.

Sufficiency of disclosure

[116] Apotex submits that the '452 patent is ambiguous because it does not teach the person skilled in the art the solvents to be used to obtain escitalopram; the suggestion being that the patent does not set out the method of using the invention in "full, clear, concise and exact" terms as contemplated by subsection 34(1) of the *Patent Act*. The Applications Judge dismissed this argument on the basis that the solvents were fully described (Reasons, para. 131). Indeed, the '452 patent indicates the concentration with which to use the solvents in question. The question whether the wording of the patent sets out the method of using the invention in sufficiently clear and exact terms is one of fact. I can see no error in the Applications Judge's conclusion on this issue.

[117] Apotex also argues that the disclosure in the '452 patent is insufficient because it lays a false trail by reason of the following statement (Reasons, para. 147): "[r]esults upon administration to human beings have been very gratifying". The Applications Judge agreed that this statement was false since escitalopram had yet to be administered to human beings at the relevant time. However, he held that (*ibidem*): "[g]iven that the patent has two full pages of evaluation of escitalopram upon rodents together with a table of pharmacological test results, I do not consider that the one-liner misled anyone. Furthermore, there is no evidence of an effort to mislead". I can see no basis for interfering with this conclusion.

[118] Apotex nevertheless argues that this does not address its contention that the invention was not correctly described and therefore is in breach of section 34 of the *Patent Act*. In my respectful

view, it was open to the Applications Judge to hold that as no one was misled, the invention was correctly described.

Procedural fairness and adequacy of reasons

[119] Genpharm submits that the Applications Judge erred in considering evidence from other proceedings and also takes issue with the fact that he rendered one set of reasons to dispose of the three applications. With respect to the evidence, Genpharm contends that the Applications Judge could not, on the record as constituted in the application that relates to it, find that 100 milligrams were necessary for the testing required by the '452 patent, that 40,000 runs would be necessary to obtain a sufficient quantity of material (Reasons, para. 112) and that Mosher's acid was not known and used as a chiral agent (Reasons, para. 110).

[120] With regard, the Applications Judge could make those findings based on the Genpharm record. On cross-examination, Dr. Newton, Genpharm's expert, acknowledged writing in a report that 100 milligrams of escitalopram would be sufficient to conduct the testing required by the '452 patent (A-135-09 Appeal Book, Vol. 29, p. 9467). The figure of 40,000 was put to Dr. Collicott, another Genpharm's expert, on cross-examination on the basis of the Rochat paper (A-135-09 Appeal Book, Vol. 28, pp. 9076 to 9083). As for Mosher's acid, although Professor Chong stated that Mosher's acid was a "standard reagent for the derivatization of chiral alcohols and amines", Dr. Newton, another expert called by Genpharm, acknowledged on cross-examination that he had never used Mosher's acid for preparative work and that prior to 1988 he had never seen Mosher's acid used in a preparative work (A-135-09 Appeal Book, Vol, 29, pp. 9533 to 9535).

[121] Turning to the adequacy of the reasons, Genpharm submits that the Applications Judge's reasons are not sufficiently intelligible to provide a basis for meaningful appellate review in that they do not adequately distinguish between the three proceedings (*Via Rail Canada Inc. v. National Transportation Agency*, [2001] 2. F.C. 25 (CA)). According to Genpharm, it is impossible to determine the basis for some of the findings made against it.

[122] During the hearing of the appeal, counsel for Genpharm gave as an example the Applications Judge's conclusion that Professor Clark's analysis was "well balanced" (Reasons, para. 111). According to counsel, such a conclusion could not have been reached on the record that relates to Genpharm. The suggestion is that the Applications Judge must have relied on evidence in the other proceedings.

[123] The argument so put does not go to the adequacy of the reasons so much as to the absence of an evidentiary foundation for the findings made. If counsel believes that the evidence does not support the Applications Judge's findings, it is incumbent upon him to make this demonstration. In this respect, the Applications Judge noted with respect to Professor Clark's evidence in the Genpharm record (Reasons, para. 111):

> … he was careful to distinguish what was known and available in 1988 as compared to later developments, with new generations of columns, with better packing material which improved resolution capacity and preparative scales. These improvements, he explained, allowed for the separation of sufficient quantities of material to allow for biological testing and not simply detection.

This finding which underlies the Applications Judge's assessment of Professor Clark's analysis is based on evidence in the Genpharm record (see A-135-09 Appeal Book, Vol. 3, pp. 467 to 470).

[124] Cobalt also takes issue with the adequacy of the reasons. For instance, it claims that in criticizing the "experts" (Reasons, paras. 103 and 106 to 109), the Applications Judge failed to particularize his complaint with the result that it is unable to determine the evidence which was relied upon in discarding the opinion of its experts. The suggestion again is that evidence from the other proceedings may have been used. However, the ultimate conclusion reached by the Applications Judge as a result of his assessment of the opinions expressed by these various experts is that citalopram could not have been resolved at the time absent inventiveness. In so holding, he relied on the evidence of Professors Davies and Clark both of whom were called by Lundbeck in the Cobalt application (Reasons, paras. 108 and 109).

[125] Along the same line, Cobalt contends that the Applications Judge used Dr. Chong's (Genpharm) critique of a study conducted by Rhodia ChiRex to find the study inconclusive. However, the Applications Judge refers to Dr. Chong as one amongst others: "Dr. Chong, <u>for one</u>, also notes …" (Reasons, para. 115 [my emphasis]). His finding, at paragraph 114, that the study did not demonstrate obviousness because it "was only a screening" and "optimization of the best candidates identified would thereafter be necessary" is supported by evidence other than Dr. Chong's critique of the study.

[126] Cobalt also takes issue with the Applications Judge's rejection of the Elati article published in 2007. In this respect, the Applications Judge did rely on admissions made by Dr. Newton (Genpharm) and Dr. McClelland (Apotex). However, he also identified grounds for rejection which are wholly independent from these admissions. The Applications Judge said, at paragraph 118, that he gave "no weight whatsoever to the Elati article" because even if it lists various ways to resolve racemates, it does not make reference to any article published before 1990 and "Elati even claims a patent on his process." He added that it "is certainly not plain and obvious that such a step would have been taken or that the Elati process would have been used" (Reasons, para. 119). Significantly, it is only after making these findings that the Applications Judge observed that "[i]n any event, there were flaws in the Elati article as admitted by Drs. Newton and McClelland" (Reasons, para. 119).

[127] As to the alleged improper use of Dr. Newton's evidence (Genpharm), the Applications Judge did rely on his assertion that when a racemic drug is ingested, its two enantiomers exist as separate compounds in solution and react with receptors within the body at different rates (Reasons, para. 126). However, he did so while discussing anticipation by prior use, an allegation that Cobalt did not pursue (Reasons, para. 125).

[128] With respect to the reliance placed by the Applications Judge on the statement by Dr. McClelland (Apotex) that he had no problem understanding the invention (Reasons, para. 142), this again was done in the context of an issue that was not raised by Cobalt, *i.e.* whether the '452 patent contained so much linguistic imperfection that it could not be understood.

[129] Cobalt makes a number of additional submissions aimed at demonstrating that it was prejudiced by the Applications Judge's decision to issue a single set of reasons. Although it would have been preferable for the Applications Judge to issue separate reasons, if only because it would have avoided this last series of attack against his judgment, I am satisfied that he was mindful of the common and distinct points raised by the appellants throughout his review and that no injustice results from the fact that he issued a single set of reasons.

[130] I would dismiss the three appeals, with costs in favour of Lundbeck in each case.

"Marc Noël"

J.A.

"I agree.
J.D. Denis Pelletier J.A."

"I agree.
Johanne Trudel J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-129-09
(APPEAL FROM A PUBLIC VERSION OF REASONS FOR ORDERS OF THE HONOURABLE JUDGE HARRINGTON OF THE FEDERAL COURT DATED FEBRUARY 25, 2009, NO. T-991-07.)	
STYLE OF CAUSE:	Apotex Inc. and Lundbeck Canada Inc. and The Minister of Health and H. Lundbeck A/S
PLACE OF HEARING:	Ottawa, Ontario
DATE OF HEARING:	September 14, 2010
REASONS FOR JUDGMENT BY:	NOËL J.A.
CONCURRED IN BY:	PELLETIER, TRUDEL JJ.A.
DATED:	November 25, 2010

APPEARANCES:

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FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-135-09

(APPEAL FROM A PUBLIC VERSION OF REASONS FOR ORDERS OF THE HONOURABLE JUDGE HARRINGTON OF THE FEDERAL COURT DATED FEBRUARY 25, 2009, NO. T-372-07.)

STYLE OF CAUSE:	Mylan Pharmaceuticals ULC (formerly Genpharm ULC) and Lundbeck Canada Inc. and The Minister of Health and H. Lundbeck A/S
PLACE OF HEARING:	Ottawa, Ontario
DATE OF HEARING:	September 14, 2010
REASONS FOR JUDGMENT BY:	NOËL J.A.
CONCURRED IN BY:	PELLETIER, TRUDEL JJ.A.
DATED:	November 25, 2010

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FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-139-09

(APPEAL FROM A PUBLIC VERSION OF REASONS FOR ORDERS OF THE HONOURABLE JUDGE HARRINGTON OF THE FEDERAL COURT DATED FEBRUARY 25, 2009, NO. T-1395-07.)

STYLE OF CAUSE:	Cobalt Pharmaceuticals Inc. and Lundbeck Canada Inc., H. Lundbeck A/S and The Minister of Health
PLACE OF HEARING:	Ottawa, Ontario
DATE OF HEARING:	September 14, 2010
REASONS FOR JUDGMENT BY:	NOËL J.A.
CONCURRED IN BY:	PELLETIER, TRUDEL JJ.A.
DATED:	November 25, 2010

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