Date: 20060213

Docket: A-431-05

Citation: 2006 FCA 64

CORAM: **RICHARD C.J.**
EVANS J.A.
PELLETIER J.A.

BETWEEN:

AVENTIS PHARMA INC.

Appellant
(Applicant)

and

APOTEX INC.
THE MINISTER OF HEALTH
and SCHERING CORPORATION

Respondents
(Respondents)

Heard at Toronto, Ontario, on January 25, 2006.

Judgment delivered at Ottawa, Ontario, on February 13, 2006.

REASONS FOR JUDGMENT BY: RICHARD, C.J.

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

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REASONS FOR JUDGMENT

RICHARD C.J.

BACKGROUND

[1] Aventis Pharma Inc. (Aventis) appeals from the Order of Justice Mactavish of the Federal Court, dated September 20, 2005 (2005 FC 1283) dismissing an application for prohibition pursuant to the *Patented Medicines (Notice of Compliance) Regulations* (Regulations) (the Prohibition Proceeding). In those proceedings, Aventis sought an Order prohibiting the Respondent, the

Minister of Health (Minister), from issuing a Notice of Compliance (NOC) to the Respondent, Apotex Inc. (Apotex), in respect of its drug product ramipril until after the expiration of Canadian Letters Patent No. 1,341,206 (the ’206 Patent). Aventis is the licensee of the ’206 Patent from the owner of the ’206 Patent and the other party in this appeal, Schering Corporation. Schering supports Aventis in this appeal.

[2] In dismissing the application for prohibition Justice Mactavish found that the Notice of Allegation by Apotex in its letter dated June 20, 2003 was a valid Notice of Allegation (NOA) as contemplated by the Regulations, and found that the allegation of invalidity of the ’206 Patent grounded on a lack of sound prediction was justified. In particular, Justice Mactavish found, as facts, that:

(a) Apotex’s Notice of Allegation detailed statement contained sufficient information to enable Aventis to knowledgeably initiate the prohibition proceeding and prepare evidence; and

(b) Schering did not have a sound basis for predicting that the compounds covered by the claims in issue in the ’206 Patent would be useful as angiotensin converting enzyme (ACE) inhibitors and in the treatment of hypertension in humans.

[3] In addition, Apotex sought to challenge the validity of the ’206 Patent on the basis that its further allegations of insufficiency of disclosure and double patenting were justified. The allegation

of double patenting was withdrawn by Apotex at the hearing of the appeal. If the above findings of Justice Mactavish are upheld there is no need to deal with the other issue.

[4] Justice Mactavish concluded, after weighing the evidence of the expert witnesses and considering the extensive evidentiary record, that Apotex's allegation as to the absence of sound prediction was justified.

THE '206 PATENT

[5] The application that resulted in the '206 Patent was filed in Canada on October 20, 1981 and issued on March 20, 2001. The patent claims priority from U.S. applications filed October 23, 1980 and April 28, 1981.

[6] The '206 Patent relates to compounds which are useful as ACE inhibitors and anti-hypertensive agents. An ACE inhibitor inhibits angiotensin-converting enzyme (ACE) which converts angiotensin I to angiotensin II. Angiotensin II increases blood pressure such that inhibition of its production reduces blood pressure. A compound that inhibits ACE is therefore useful as an anti-hypertensive agent.

NATURE OF THE PROCEEDINGS

[7] Proceedings under the NOC Regulations are not actions for the determination of patent invalidity or infringement. They are judicial review proceedings to determine whether the Minister

of Health is free to issue the requested NOC under the *Food and Drugs Act,* R.S. 1985, c. F-27. These proceedings do not deprive a patentee or licensee from asserting any rights they may have with respect to the patent by means of an action and a full trial of the issue.

BURDEN OF PROOF IN NOC PROCEEDINGS

[8] The jurisprudence of the Federal Court of Appeal clearly establishes that the onus of proof in NOC proceedings rests on the applicant and is considered on a balance of probabilities, bearing in mind that on allegations of invalidity, there is a statutory presumption of validity in favour of the patentee.

[9] Aventis and Schering argue that an attack on the validity of a patent is a collateral challenge to the Commissioner's decision to issue the patent, and that the standard of review of that decision is unreasonableness *simpliciter*, where, as here, the question in dispute is one of mixed fact and law: (see *Apotex Inc. v. Wellcome Foundation Ltd*., [2002] 4 S.C.R. 153 at paras. 42-44; *Schmeiser v. Monsanto Canada Inc.*, [2004] 1 S.C.R. 902 at para. 24.) This principle, they say, is equally applicable to NOC proceedings when the NOA alleges, as here, that the first person's patent is invalid.

[10] I do not agree. As I have already stated, NOC proceedings are summary and do not determine the validity of a patent, but only whether the NOA is justified, and an order of prohibition should issue. The fact that a NOA may call the validity of a patent into question for the purpose of a NOC proceeding is not sufficient to attract the more onerous standard of proof applicable when the

validity of the patent is determined in an infringement action. (See for example, *Janssen Ortho Inc. v. Novopharm Ltd*. (2004), 35 C.P.R. (4th) 353, 2004 FC 1631 at para. 21 (FC)).

SUFFICIENCY OF THE NOA

[11] Aventis/Schering contend that Justice Mactavish erred by finding that Apotex's NOA, with respect to sound prediction, was legally sufficient.

[12] I am satisfied that Justice Mactavish properly determined the claim of sufficiency of Apotex's NOA, based on the jurisprudence of this Court and on the evidentiary record.

[13] A NOA accompanied by a detailed statement is adjudged sufficient if it allows the patentee to decide, in light of the scope of its patent and the alleged basis of invalidity, whether to institute an application to prohibit the issue of an NOC. Whether the detailed statement in the NOA is sufficient is a question of mixed fact and law. As such, this Court may only interfere with the Judge's conclusion that the NOA was sufficiently detailed to comply with paragraph 5(3)*(a)* if it is satisfied that the decision is vitiated by some palpable and overriding error. (*Pfizer Canada Inc. v. Apotex Inc*, 38 C.P.R. (4th) 400 at para 25 (F.C.A.); *AstraZeneca AB v. Apotex Inc.*, [2005] F.C.J. No. 842 at para. 9 (F.C.A.) (*AstraZeneca AB*)).

[14] A detailed statement will meet the legal requirement for adequacy if it provides the patent holder with sufficient understanding of the case it has to meet. Justice Mactavish found that

Apotex's NOA/detailed statement provided sufficient information upon which Aventis could evaluate the allegation and commence this proceeding.

[15] She specifically considered the sufficiency of Apotex's NOA as it relates to the issue of sound prediction. She applied the test set out in *Novopharm Ltd. v. Pfizer Canada Inc.*, [2005] F.C.J. No. 1318, and found as fact that Apotex's NOA put Aventis on notice of the sound prediction argument.

[16] Aventis/Schering specifically focus on the words "requisite level of activity" in the NOA. Justice Mactavish determined that "level of activity" relates to the potency of the compounds in question and therefore whether the compounds lacked any activity at all. In addition, Justice Mactavish considered the lack of an affidavit filed on behalf of Aventis with respect to the alleged lack of specificity in the Apotex NOA to be telling, as per *AstraZeneca AB.*

[17] The decision of Justice Mactavish was supported by the evidentiary record. As Justice Mactavish made no palpable and overriding error, her determination with respect to the sufficiency of Apotex's NOA should not be interfered with.

STANDARD OF REVIEW

[18] In *Elders Grain* Co. *v. M/V Ralph Misener (The)*, [2005] F.C.J. No. 612, I had the opportunity to review the standard of review of an appellate court from a decision made by a court of first instance and which are applicable in the circumstance of this appeal:

> [6] It is settled law that an appeal is not a trial *de novo*. The role of an appellate court is not to write a better judgment than the trial judge but to review his or her reasons in light of the arguments of the parties and the relevant evidence. Therefore, this Court must give consideration to the standard of review applicable to the various issues which arise on this appeal: *Housen v. Nikolaisen*, [2002] 2 S.C.R. 235.
>
> [7] In *Housen*, the Supreme Court of Canada set out the standards of review to be used by an appellate court in regards to the following types of questions: (1) questions of law; (2) questions of fact; (3) inferences of fact, and (4) questions of mixed fact and law.
>
> [8] The standard of review for pure questions of law is correctness and an appellate court is therefore free to replace the opinion of the trial judge with its own.
>
> [9] The standard of review for findings of fact is that such findings are not to be reversed unless it can be established that the trial judge made a "palpable and overriding error".
>
> [10] Justice Bastarache in *Van de Perre v. Edwards*, [2001] 2 S.C.R. 1014 at paragraph 15 defined a palpable and overriding error as one "that gives rise to the reasoned belief that the trial judge must have forgotten, ignored or misconceived the evidence in a way that affected his conclusion." In short, a palpable and overriding error is an obvious deficiency in the trial judge's findings of fact that affects the outcome of the trial.
>
> [11] Accordingly, this Court must review the trial judge's decision on a standard of correctness for pure questions of law. Regarding findings of fact and inferences of fact, this Court must exercise the utmost deference, disturbing the trial judge's decision only in the presence of palpable and overriding error.
>
> [12] A determination that involves the application of a legal test to a set of facts is a question of mixed fact and law. That determination is subject to a standard of palpable and overriding error unless it is clear that the trial judge made some extricable error in principle with respect to the characterization of the legal test or its application, in which case the error may amount to an error of law: *Housen, supra* at paragraph 37; *R. v. Buhay*, [2003] 1 S.C.R. 631 at paragraph 45.

[19] In the later case of *H.L. v. Canada (Attorney General)*, [2005] 1 S.C.R. 401, Chief Justice McLachlin, re-visited the *Housen* decision and commented:

> [9] […] this Court in *Housen* was unanimous on the issue that concerns us here: All nine Justices agreed that the standard of appellate review on questions of fact in Saskatchewan is review for error and not review by rehearing. They agreed as well that findings of fact by the trial judge will be disturbed on appeal only for errors that can properly be characterized as palpable and overriding.
>
> [10] It was not contended in *Housen*, either in the Saskatchewan Court of Appeal or in this Court, that the standard of appellate review in Saskatchewan differed significantly from the prevailing standard elsewhere in Canada.

[20] She added:

> "Doubt as to the soundness of the trial judge's findings of fact, however, is not a recognized ground of appellate intervention."

[21] She noted:

> [53] The standard of review for error has been variously described. In recent years, the phrase "palpable and overriding error" resonates throughout the cases. Its application to all findings of fact — findings as to "what happened" — has been universally recognized; its applicability has not been made to depend on whether the trial judge's disputed determination relates to credibility, to "primary" facts, to "inferred" facts or to global assessments of the evidence.

[22] In the absence of any statutory direction, it is not the role of appellate courts to rehear or retry cases.

[23] It is this standard of appellate review which must be applied in this appeal.

SOUND PREDICTION

[24] To be patentable, an invention must be useful. However, even if the utility of one or more elements in the claim was not demonstrated or known at the time of claiming, such a claim may nevertheless be upheld if it can be shown that the inventor could make a "sound prediction" that the elements in question, if made, would prove to be useful for their stated purpose.

[25] While utility may be established through testing an invention, it is well established that complete testing is not essential if the utility of a patent claim can be soundly predicted based upon available information and expertise (*Apotex Inc. v. Wellcome Foundation Ltd.*, [2002] 4 S.C.R. 153 (*Apotex)*).

[26] If it is shown that the inventor could not make a sound prediction that something he claimed to have invented, but had not actually made or shown to be useful, would be useful, the claim will be invalid.

[27] The Supreme Court, in *Apotex*, supra, set out a three part test to determine if a prediction is sound:

(a) First, there must be a factual basis for the prediction. The factual basis may be established by supplying the tested compounds (See *Monsanto Canada Inc. v. Schmeiser*, [2004] 1 S.C.R. 902); although other factual findings may be adequate;

(b) Second, the inventor must have at the date of the patent application an "articulable" and "sound" line of reasoning from which the desired result can be inferred from the factual basis; and

(c) Third, there must be proper disclosure.

[28] As noted by Justice Binnie at paragraph 66:

> "The doctrine of 'sound prediction' balances the public interest in early disclosure of new and useful inventions, even before their utility has been verified by tests (which in the case of pharmaceutical products may take years) and the public interest in avoiding cluttering the public domain with useless patents, and granting monopoly rights in exchange for misinformation."

[29] The soundness of a prediction is a question of fact and is to be assessed based upon information and expertise available at the relevant time.

[30] I am in agreement with Justice Mactavish that the relevant date is the Canadian filing date, in this case, October 20, 1981. It is the time which is most reasonable in achieving consistency in the application of the three components of the *Wellcome* test.

[31] Justice Mactavish applied the three components of the legal test and found, on the basis of the record before her, that Aventis/Schering could not rely on the doctrine of sound prediction to satisfy the statutory test of "utility".

[32] She found that the Appellants could not satisfy any of the three elements required by the *Wellcome* test concerning Claim 12 of the '206 Patent and, given that the compounds included in Claim 12 were also included in Claims 1,2,3 and 6 of the patent, the same conclusion applied to those claims.

[33] With respect to the first two parts of the *Wellcome* test, Justice Mactavish found that Schering's prediction was not supported by a factual basis nor an articulable line of reasoning.

[34] With respect to the last part of the *Wellcome* test, the requirement of proper disclosure, Justice Mactavish found that, based on the state of the knowledge in October 1981, the disclosure with respect to Claim 12 of the '206 Patent was insufficient.

[35] Even if this Court was to find that Justice Mactavish erred in determining that Aventis/Schering did meet the third factor of the *Wellcome* test on the disclosure requirement, the allegation that the patent is invalid would still be justified because all three parts of the test must be satisfied.

EVIDENCE OF DR. MARSHALL

[36] Justice Mactavish found that the inventors of the '206 Patent did not have a sound basis for predicting that the eight compounds covered by claim 12 would be useful as ACE inhibitors and as anti-hypertensive agents, and on this basis dismissed the application.

[37] Aventis and Schering argue that Justice Mactavish erred in preferring the evidence of Dr. Marshall over the evidence of their witnesses, Drs. Triggle and Silverman.

[38] She considered Aventis and Schering's submission that Dr. Marshall set the bar too high in relation to the test for sound prediction – that he was looking for a certainty. However, she was

satisfied from reviewing Dr. Marshall's evidence, in its entirety, that he properly understood the test in issue in this regard.

[39] She also accepted that in some places in his evidence, Dr. Marshall was examining the issue of utility from the perspective of whether the compounds created by the Schering scientists had potential use as ACE inhibitors and anti-hypertensive agents in the commercial sense of the word.

[40] She did have some concerns with respect to Dr. Marshall's evidence regarding the need to test for things such as toxicity in order to be able to make a sound prediction but did not view that as otherwise undermining the weight to be attributed to his evidence.

[41] She observed that the fact that Dr. Marshall may have looked to commercial utility at some points in his evidence in no way takes away from the validity of Dr. Marshall's conclusion that there was simply not enough known about the chirality or stereochemistry of the compounds tested by Schering in the period leading up to the Canadian filing in October of 1981 so as to be able to predict whether the compounds coming within Claim 12 of the '206 Patent would exhibit any activity. This conclusion was one entirely within Dr. Marshall's field of expertise, and for the three reasons she articulated, she preferred Dr. Marshall's evidence in this regard to that of Drs. Triggle and Silverman.

[42] First, she notes that Dr. Marshall was the only witness to have devoted his entire academic career to the study of ACE inhibitors, specifically, having been published and having received international recognition for his work in this area.

[43] Second, Justice Mactavish explains that the affidavit of Dr. Marshall presented a much more detailed and complete explanation and analysis of the issue at bar than was offered in the affidavits of the two other witnesses.

[44] Finally, Justice Mactavish indicates that she preferred Dr. Marshall's evidence over Dr. Triggle's evidence as the affidavit presented by Dr. Triggle in this case was almost identical to the one sworn by him on behalf of Aventis in another proceeding involving the same patent (*Aventis Pharma Inc. v. Pharmascience Inc.*, [2005] F.C.J. No. 511,) (Aventis), except for one important material distinction.

[45] Three paragraphs included in the affidavit filed in *Aventis* had been deleted before his affidavit was filed in this case and, according to Justice Mactavish, the three paragraphs were significant in that they partially corroborated the evidence presented by Dr. Marshall regarding the possibility to predict qualitatively or quantitatively biological activity between different isomers.

[46] Justice Mactavish considered all the evidence in the record and made a factual determination with respect to what she considered was the best evidence on which to found her decision based on the *Wellcome* Test of sound prediction.

RESULT

[47] In applying the proper standard of appellate review to the decision under appeal, I have concluded that Justice Mactavish had an ample evidentiary basis to support her decision that the inventors at Schering could not, at the Canadian filing date, soundly predict the usefulness of the compounds in claim 12 of the ’206 Patent for their stated purpose, nor could they predict the usefulness of the members of the class of compounds claimed in claims 1, 2, 3 and 6.

[48] There was substantial evidentiary basis for her findings. In making these findings, she made no overriding and palpable error.

[49] Accordingly the appeal will be dismissed with one set of costs to the Respondent Apotex.

“J. Richard”

C.J.

“I agree
John M. Evans J.A.”.

“I agree
J.D.Denis Pelletier J.A.”.

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-431-05
(APPEAL FROM A JUDGMENT OF THE HONOURABLE MADAM JUSTICE MACTAVISH OF THE FEDERAL COURT DATED SEPTEMBER 20, 2005, COURT FILE NO. T-1742-03)	
STYLE OF CAUSE:	Aventis Pharma Inc. v.Apotex Inc., The Minister of Health and Schering Corporation
PLACE OF HEARING:	Toronto, Ontario
DATE OF HEARING:	January 25, 2006
REASONS FOR JUDGMENT BY:	RICHARD, J.C.
CONCURRED IN BY:	EVANS J.A. PELLETIER J.A.
DATED:	February 13, 2006

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