Federal Court of Appeal | Cour d'appel fédérale

Date: 20100729

Docket: A-281-09

Citation: 2010 FCA 204

CORAM: **NADON J.A.**
SHARLOW J.A.
LAYDEN-STEVENSON J.A.

BETWEEN:

PFIZER LIMITED

Appellant

and

RATIOPHARM INC.

Respondent

Heard at Ottawa, Ontario, on June 24, 2010.

Judgment delivered at Ottawa, Ontario, on July 29, 2010.

REASONS FOR JUDGMENT BY: **LAYDEN-STEVENSON J.A.**

CONCURRED IN BY: NADON J.A.
SHARLOW J.A.

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REASONS FOR JUDGMENT

LAYDEN-STEVENSON J.A.

[1] The respondent (Ratiopharm), pursuant to the provisions of the *Patent Act*, R.S.C. 1985, c. P.4 (the Act), commenced an action in the Federal Court with respect to the appellant's (Pfizer) Canadian Letters Patent No. 1,321,393 (the '393 Patent). Ratiopharm requested, among other things, a declaration that the '393 Patent is invalid. A Federal Court judge (the trial judge) granted Ratiopharm's request.

[2] Following a four-week trial involving 20 witnesses (eight of whom were experts), the trial judge concluded that the '393 Patent is invalid for obviousness. He also found, in *obiter*, that the patent is invalid on a number of other grounds. Specifically, he found: the '393 Patent lacked utility; its disclosure was insufficient; it was misleading and invalid under section 53 of the Act; and it failed to meet the criteria for a valid selection patent.

[3] Pfizer appeals from the Federal Court judgment. To succeed, Pfizer must demonstrate a reviewable error with respect to each of the grounds upon which the trial judge ruled. For the reasons that follow, I have not been persuaded that the trial judge erred in concluding that the '393 Patent was obvious. Consequently, Pfizer's appeal must fail.

Amlodipine besylate

[4] The '393 Patent is entitled "Besylate Salt of Amlodipine". Only Claim 11 is in issue. That claim reads: "The besylate salt of amlodipine." Amlodipine was invented by Pfizer. It is a calcium channel blocker and is an anti-hypertensive compound. A broad class of amlodipine and its pharmaceutically acceptable acid addition salts were disclosed in Pfizer's prior European Patent Application 089167 (EP 167). Amlodipine besylate, marketed under the tradename NORVASC, is used to treat high blood pressure and angina. The therapeutic effects of amlodipine besylate are provided by amlodipine.

[5] Before a drug can be sold, it must be produced in a form suitable for manufacture, storage,

transportation and administration to patients. The properties required to achieve a pharmaceutically acceptable form include solubility (absorption into the patient's bloodstream), stability (minimal changes during manufacture), non-hygroscopicity (attracts little water) and processability (does not stick to manufacturing equipment).

[6] To achieve these properties, it is often necessary to convert the free base drug into a salt. A salt is an ionic compound that is formed when a base (such as amlodipine) is combined with an acid. The '393 Patent covers the besylate salt (benzene sulphonate, a sulphonic acid) of amlodipine. It is common ground that amlodipine besylate is a pharmaceutically acceptable salt.

Development of amlodipine besylate

[7] Pfizer initially attempted to formulate amlodipine in the form of the maleate salt. However, during the regulatory approval process, amlodipine maleate exhibited problems with stability and processability. Consequently, Pfizer began to search for a different salt of amlodipine through an accepted process known as salt screening. Pfizer tested seven salts: acetate, succinate, mesylate, besylate, salicylate, hydrochloride and tosylate. It decided to proceed with the besylate salt. The trial judge described the salt screening process at paragraph 50 of his reasons:

> [T]he procedure followed by [Pfizer scientists] Dr. Wells and Mr. Davison was essentially a classic mid 1980s salt screening process for a pharmaceutical candidate…It was somewhat rough and ready, time was an essential constraint, certain salts only were selected, not entirely at random, for testing. Once one or two or three sufficiently useful candidates were identified, there was no effort to test all possible salts. The selected candidate(s) were settled upon and passed on to the next stage, that of final formulation for regulatory approval.

[8] In a memorandum dated 25 November 1985, Pfizer scientist and inventor Dr. James Wells described his findings in contemplation of a patent. The content of the memorandum is quoted at paragraph 103 of the trial judge's reasons:

> We recommend a patent filing to protect the besylate and tosylate salts of UK-48,340 because there is:
>
> (a) improved shelf life of solid dosage forms due to improved solid state stability of the besylate and tosylate salts;
>
> (b) improved processing of tablets and capsules because sticking is considerably reduced by the besylate and tosylate salts. This allows economic tableting by direct compression whereas although wet massing reduces stickiness it compromises stability;
>
> The mesylate salt probably also merits protection since its stability and processing properties are excellent. However, it is isolated in the anhydrous form and upon exposure to moisture rises rapidly to the monohydrate. The besylate and tosylate are however non-hygroscopic and anhydrates.

The memorandum refers to the improvements (advantages) of amlodipine besylate and other sulphonates.

[9] Pfizer filed its Canadian patent application on April 2, 1987, claiming priority from its UK patent application filed on April 4, 1986. The '393 Patent issued on August 17, 1993 and will expire on August 17, 2010. It is a selection patent.

The Trial Judge's Reasons

[10] The trial judge provided detailed, cogent and articulate reasons for his findings. He identified and described each witness and his impression of the witness's testimony. He noted the

conflicting expert evidence, stated which evidence he preferred and provided the reasons for his preferences.

[11] He described the qualifications of the person skilled in the art (POSITA) and identified the relevant dates for the application of the POSITA's evidence. He construed the pertinent claim and concluded that the claimed invention is "a particular salt form, besylate, of a known pharmaceutical compound, amlodipine." The claim is "unrestricted as to any particular use and unrestricted as to any particular form of the compound."

[12] The trial judge discussed the development of pharmaceutical products in the 1980s, particularly the stage known as salt selection or salt screening, and included references to the testimony of the witnesses. Then, in 55 paragraphs, he detailed the development and patenting of amlodipine besylate, again with references to the evidence. He construed the promise of the patent and found it promised that besylate amlodipine possessed a unique combination of properties making it particularly and outstandingly suitable for preparation of pharmaceutical formulations of amlodipine. Next, he devoted an additional 40 paragraphs to a comparison between what the '393 Patent said and "what actually happened" and made a number of factual conclusions which he set out at paragraph 153 of his reasons. He then turned to the legal issues, the first of which was obviousness.

The Standard of Review

[13] The standard of review is articulated in *Housen v. Nikolaisen,* [2002] 2 S.C.R. 235. There,

the Supreme Court reiterated that an appeal is not a re-trial of a case. Questions of law are to be determined on a standard of review of correctness. This means that an appellate court is at liberty to replace the opinion of the trial judge with its own. The standard of review for findings of fact is palpable and overriding error, that is, the factual findings cannot be reversed in the absence of an error that is plainly seen.

Obviousness

The Trial Judge's Reasoning

[14] In addressing the issue of obviousness, the trial judge acknowledged that he must look at the claim as properly construed. At paragraph 159 of his reasons, he set out the approach to obviousness adopted by the Supreme Court of Canada in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, [2008] 3 S.C.R. 265 (*Sanofi*):

> (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 claims 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?

[15] The trial judge, at paragraph 160 of his reasons, specified the questions that provide guidance at the fourth stage of the *Sanofi* approach when the court ascertains whether an invention is "obvious to try":

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?

He then noted this Court's decision in *Apotex Inc. v. Pfizer Canada Inc.*, [2004] 4 F.C.R. 223 and correctly concluded that "worth a try" and "obvious to try" are not synonymous.

[16] The trial judge summarized the relevant circumstances at paragraphs 167 and 168 of his reasons and concluded that what Pfizer had done was routine for a POSITA at the time. He further concluded that the claimed invention, a besylate salt of amlodipine, was obvious.

Pfizer's Allegations of Error

[17] Pfizer alleged that the trial judge erred in two respects. It characterized one error as a legal error and the other as a palpable and overriding factual error. Regarding the factual error, Pfizer asserted that the trial judge erred in finding the POSITA "would have had every reason to test the besylate salt." Pfizer complained that its cross-examination of Dr. Cunningham (where Pfizer ostensibly demonstrated that the six pieces of art referred to by Dr. Cunningham did not support such a conclusion) was either forgotten or ignored by the trial judge. This, in Pfizer's view, ascended to the level of palpable and overriding error.

[18] The alleged legal error related to the manner in which the trial judge applied, as Pfizer put it, the "test for obviousness" as enunciated by *Sanofi*. Specifically, in its written submissions, Pfizer argued that the trial judge erred by focussing on the process the inventors used in developing the invention rather than the outcome or result of the process. Pfizer submitted that, when an invention is arrived at through testing, it is not necessarily obvious merely because the utilized tests were within the knowledge and capacity of the POSITA. The invention is obvious only if its result was obvious.

[19] Pfizer accepted that mere verification of known properties of a common substance does not constitute an invention and therefore cannot be patented, but it relied on the statement of this Court in *Pfizer Canada Inc. v. Canada (Minister of Health)*, 2006 FCA 214, [2007] 2 F.C.R. 137 *(Pfizer NOC)* that "the formulation properties of any salt of amlodipine could never have been expected but must be determined empirically." It contended that the trial judge simply adopted the findings of the United States Court of Appeals for the Federal Circuit in *Pfizer Inc. v. Apotex Inc.* (2006), 480 F. 3d 1348 *(U.S. authority)* that "it was routine in the art to verify the expected physiochemical characteristics of each salt…and Pfizer's scientists used standard techniques to do so." Thus, according to Pfizer, the trial judge's error was based on this erroneous reliance and required the intervention of this Court.

[20] At the hearing, counsel for Pfizer suggested that the question for obviousness fell to be determined by asking whether there was mere verification or whether there was inventiveness. If there was more than mere verification, then there is an invention and no obviousness. The two sides

of the equation were said to be mutually exclusive. Counsel reiterated the relevant question as whether the result (rather than the process) was more or less self-evident, that is, was it predictable?

[21] In sum, Pfizer maintained that the trial judge asked whether the process was more or less self-evident (or predictable) when the appropriate question was whether the result was self-evident (or predictable). Accordingly, in Pfizer's view, the trial judge misdirected himself as to the law.

Analysis

[22] The alleged factual error can be addressed summarily. I agree with Ratiopharm that Dr. Cunningham's evidence was based not only on the art, but on his experience in the industry, his knowledge with respect to salt selection and the functionalities of various known groups of salts. Further, Dr. Atwood's evidence corroborated that of Dr. Cunningham.

[23] At its core, this alleged error is a complaint that the trial judge was insufficiently persuaded by Pfizer's cross-examination. It does not demonstrate palpable and overriding error.

[24] Pfizer's argument that the trial judge erroneously relied upon and adopted the conclusion from the *U.S. authority* ties into its argument with respect to mere verification and obviousness.

[25] First, Pfizer grounds its position on a factual conclusion from *Pfizer NOC*, a case arising out of the *Patented Medicine Notice of Compliance Regulations*, S.O.R./93-133 (NOC Regulations). This Court has repeatedly stated that what I will refer to as "NOC proceedings" do not operate as

res judicata. While Pfizer may be correct that the factual basis in the NOC proceeding is the same as that in this action, it does not follow that the evidentiary basis is the same. Factual findings are derived from the evidence that is before the court in the particular proceeding.

[26] The trial judge was aware of the previous NOC proceedings in relation to the '393 Patent and considered them to be instructive (reasons at para. 18). However, he was not and could not be bound by the factual determinations in a prior NOC proceeding. Rather, it was incumbent upon the judge to arrive at his findings on the basis of the evidence that was before him.

[27] Second, it is clear that the trial judge properly identified the legal criteria set out in *Sanofi* regarding the "obvious to try" issue. The criteria in this respect are concerned with the solution (or result). Because the '393 Patent is a selection patent, the result to be assessed is the advantage(s) of amlodipine besylate over amlodipine and its maleate salts. It does not necessarily follow from the trial judge's factual finding, that the properties of the besylate salt could not have been predicted, that there must have been more than "mere verification." Parenthetically, I note that, although Pfizer relies heavily on the term "mere verification", there is no reference to it in the trial judge's analysis.

[28] The pivotal factual finding that the result of the besylate salt screening (its advantages) was predictable or obvious to try is found at paragraph 170 of the trial judge's reasons where he stated:

> I agree in particular with Dr. Cunningham in his conclusions as set out in paragraph 179 of his report, Exhibit 17, a person skilled in the art would be motivated to test sulphonic acid salts in general and would have every reason to test the besylate salt as this had already been shown to offer advantages over other salts in terms of stability.

[29] This factual determination is sufficient to dispose of Pfizer's argument. However, I also disagree that the trial judge adopted the findings contained in the *U.S. authority*. Early in his reasons, the trial judge noted that the United States authorities were not binding and were based on law that may in some respects be different than Canadian law (reasons at para. 17).

[30] More importantly, it is readily apparent from his reasons that the trial judge independently arrived at his conclusion with respect to whether the testing of the besylate salt and the result was obvious to try. After making that factual finding, he noted that the U.S. Court of Appeals had reached the same determination. The trial judge's observation does not constitute either reliance or adoption. Technically, his comment in this respect is *obiter*.

[31] In summary, Pfizer's arguments essentially amount to a disguised attempt to challenge factual determinations by characterizing them as errors of law. Pfizer has not persuaded me that the trial judge made any palpable and overriding error with respect to his factual findings. There was an evidentiary basis upon which the findings could be made. Nor have I been persuaded, for the foregoing reasons, that the trial judge erred in law.

Alternative Grounds

[32] It is not necessary to address in detail the trial judge's alternative grounds for invalidating the '393 Patent. However, two observations are in order.

[33] In relation to the ground entitled “Selection Patent” in his reasons, the trial judge expressed reservation as to whether a category of “selection” patent exists (reasons at para. 180). He concluded that, if it did, the patent is invalid for this reason as well. This Court has since released its reasons for judgment in *Eli Lilly Canada Inc., v. Novopharm Limited*, 2010 FCA 197 and has determined that the conditions for a valid selection patent do not constitute an independent basis upon which to attack the validity of a patent.

[34] Pfizer expressed concern that the trial judge’s determination pursuant to subsection 53(1) of the Act was based on an overly broad interpretation of that subsection. I am of the view that the determination is confined to the unique and particular circumstances of this matter. It has limited, if any, value as a precedent.

Conclusion

[35] I would dismiss the appeal with costs to Ratiopharm.

"Carolyn Layden-Stevenson"
J.A.

“ I agree
M. Nadon J.A.”

“I agree
K. Sharlow”

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-281-09
APPEAL FROM A JUDGMENT OF THE FEDERAL COURT DATED July 8, 2009, Court File NO. T-1712-07	
STYLE OF CAUSE:	Pfizer Limited v. Ratiopharm Inc.
PLACE OF HEARING:	Ottawa, Ontario
DATE OF HEARING:	June 24, 2010
REASONS FOR JUDGMENT BY:	**LAYDEN-STEVENSON J.A.**
CONCURRED IN BY:	**NADON J.A.** **SHARLOW J.A.**
DATED:	July 29, 2010

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