Federal Court of Appeal | Cour d'appel fédérale

Date: 20110317

Docket: A-22-10

Citation: 2011 FCA 102

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

BETWEEN:

PHARMASCIENCE INC.

Appellant

and

PFIZER CANADA INC., PHARMACIA ATKIEBOLAG and THE MINISTER OF HEALTH

Respondents

Heard at Montréal, Quebec, on February 23, 2011.

Judgment delivered at Ottawa, Ontario, on March 17, 2011.

REASONS FOR JUDGMENT BY: NOËL J.A.

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

Federal Court of Appeal | Cour d'appel fédérale

Date: 20110317

Docket: A-22-10

Citation: 2011 FCA 102

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

BETWEEN:

PHARMASCIENCE INC.

Appellant

and

PFIZER CANADA INC., PHARMACIA ATKIEBOLAG and THE MINISTER OF HEALTH

Respondents

REASONS FOR JUDGMENT

NOËL J.A.

[1] This is an appeal from a judgment of Heneghan J. of the Federal Court (the Applications Judge), wherein she granted the application brought by Pfizer Canada Inc. and Pharmacia Atkiebolag (the respondents) to prohibit the Minister of Health (the Minister) from issuing a Notice of Compliance (NOC) to Pharmascience Inc. (the appellant) pursuant to section 6 of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, until the expiry of Canadian Patent No. 1,339,132 (the '132 Patent).

[2] The ‘132 Patent claims, *inter alia*, a compound known as latanoprost for use in the treatment of glaucoma and ocular hypertension. A 50 microgram/ml ophthalmic solution of latanoprost is marketed in Canada under the name Xalatan®.

[3] A Notice of Allegation (NOA) was served on the respondents on November 2, 2007. In it, the appellant alleged that the ‘132 Patent was invalid on eleven grounds including anticipation, lack of utility, and the failure to soundly predict the “invention”. The appellant also alleged that whether the patent was valid or not, its version of latanoprost would not infringe the patent.

[4] On December 20, 2007, the respondents sought an order prohibiting the Minister from issuing a NOC to the appellant. Following a three-day hearing, the Applications Judge held that none of the allegations made in the NOA had been established and issued the prohibition order. The appellant maintains that in so holding, the Applications Judge made a number of legal and factual errors.

[5] For the reasons which follow, I am of the view that the appeal should be dismissed.

FACTUAL BACKGROUND

The ‘132 Patent

[6] The ‘132 Patent is entitled “Prostaglandin Derivatives for the Treatment of Glaucoma or Ocular Hypertension”. It was filed on September 12, 1989 – it thus falls under the purview of the *Patent Act*, R.S.C. 1985, c. P-4, as it read prior to October 1, 1989 – and was issued on July 29,

1997. The patent addresses certain prostaglandin derivatives and their use in the treatment of glaucoma or ocular hypertension.

[7] Prostaglandins are naturally occurring substances found in human and animal tissues. $PGF_{2\alpha,}$ is a type of prostaglandin that can be esterified into $PGF_{2\alpha}$-isopropyl ester. Latanoprost, the compound claimed in the '132 Patent, is a prostaglandin derivative that has the following chemical formula: 13,14-dihydro-17-phenyl-18,19,20-trinor $PGF_{2\alpha}$-isopropyl ester. Latanoprost is obtained by modifying $PGF_{2\alpha}$ in the following manner (reasons at para. 6):

i. removing the last 3 carbons of the omega chain ("18,19,20-trinor");
ii. attaching a phenyl ring to carbon 17 ("17-phenyl");
iii. changing the double bond to a single bond between carbon 13 and carbon 14 ("13,14-dihydro"); and
iv. esterifying the carboxylic acid to an isopropyl ester.

[8] The '132 Patent contains 38 claims. On appeal, only claims 12, 19, 31, 37 and 38 are at issue. Claim 12 claims a composition and is dependent on claim 1, claim 19 is a compound *per se* claim that depends on claim 18, and claims 31, 37 and 38 claim various uses. The relevant claims read as follows:

> 1. A therapeutic composition for topical treatment of glaucoma or ocular hypertension, containing a prostaglandin PGA, PGB, PGD, PGE or PGF in an amount sufficient to reduce intraocular pressure without causing substantial ocular irritation and an ophthalmologically compatible vehicle, which the omega chain of the prostaglandin has the formula:
>
> (13) (14) (15-24)
> C - B - C - D - R_2
>
> wherein
> C is a carbon atom (the number is indicated within parenthesis);

B is a single bond, a double bond or a triple bond;
D is a chain with 1-10 carbon atoms, optionally interrupted by hetero atoms O, S, or N, the substituents on each carbon atom being H, alkyl groups, lower alkyl groups with 1 – 5 carbon atoms, an oxo functionality or a hydroxyl group;
R_2 is a ring structure selected from the group consisting of phenyl and phenyl having at least one substituent, said substituent being selected from C_1-C_5 alkyl groups, C_1-C_4 alkoxy groups, trifluoromethyl groups, C_1-C_3aliphatic acylamino groups, nitro groups, halogen atoms, and phenyl group; or an aromatic heterocyclic group having 5-6 ring atoms, selected from the group consisting of thiazol, imidazole, pyrrolidine, thiopene and oxazole; or a cycloalkane or a cycloalkene with 3-7 carbon atoms in the ring, optionally substituted with lower alkyl groups with 1-5 carbon atoms.

12. An ophthalmological composition according to claim 1, wherein the prostaglandin derivative is 13,14-dihydro-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$ - isopropylester.

18. 13,14-dihydro-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$-alkyl-ester, in which the alkyl group has 1-10 carbon atoms.

19. Compound of claim 18, wherein the alkyl group is isopropyl.

31. The use of 13,14-dihydro-17-phenyl-18, 19,20-trinor-$PGF_{2\alpha}$-isopropylester in the treatment of glaucoma or ocular hypertension.

37. The use of 13,14-dihydro-17-phenyl-18,19,20-trinor- $PGF_{2\alpha}$-alkyl-ester, in which the alkyl group has 1-10 carbon atoms for the treatment of glaucoma or ocular hypertension.

38. The use of 13,14-dihydro-17-phenyl-18,19,20-trinor- $PGF_{2\alpha}$-isopropyl-ester in the treatment of glaucoma or ocular hypertension.

[9] The promised utility – *i.e.* the treatment of glaucoma or ocular hypertension without substantial ocular irritation – is based *inter alia* on test results from three animal models and human tests conducted on employees of Pharmacia Atkiebolag, one of the respondents (‘132 Patent at pp. 18-29).

The eye, glaucoma and ocular hypertension

[10] The eye is a closed sphere that produces a clear fluid called aqueous humor. This fluid is essential to the functioning of the eye as it conveys nutrients to the eye and removes waste products and contaminants. The drainage of aqueous humor assists in avoiding an increase in intraocular pressure.

[11] An elevated intraocular pressure is one of the strongest risk factors for disorders of the eye, including glaucoma and ocular hypertension. Ocular hypertension consists of an intraocular hypertension without damage to the optic nerve. Glaucoma is a group of disorders characterized by damage to the optic nerve that results in a loss of vision if the condition is left untreated. There is no cure for glaucoma. However, it and ocular hypertension can be managed by reducing intraocular pressure, which can be achieved with drugs in one of two ways: production of aqueous humor or increase in the outflow of aqueous humor. Latanoprost is the first compound which treats glaucoma by increasing the rate at which aqueous humor is drained from the eye.

[12] The successful management of glaucoma by drugs requires a high level of patient compliance. Therapies with less frequent dosage contribute to a higher level of patient compliance as does the tolerability of the drug used. According to the inventors, there were a number of drugs on the market for glaucoma and ocular hypertension prior to the introduction of latanoprost. However they also had numerous undesirable effects. Latanoprost was claimed as a new substance which treats glaucoma and ocular hypertension without causing substantial ocular irritation.

DECISION OF THE FEDERAL COURT

[13] The Applications Judge began by summarizing the evidence including the expert testimony of Drs. Mitra, Podos, Prestwich and Spaeth on behalf of the appellant and Drs. Buys, Fechtner, Stjernschantz, Maxey and Neufeld on behalf of the respondents. After having outlined the anatomy of the eye – as just summarized (paras. 10-12) – and identified the issues as they arise within the framework of the NOC Regulations, she turned to the construction of the '132 Patent.

[14] Relying on the principles of claim construction set out by the Supreme Court of Canada in *Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, [2000] 2 S.C.R. 1067 and *Free World Trust v. Électro Santé Inc.*, 2000 SCC 66, [2000] 2 S.C.R. 1024, the Applications Judge construed claims 12, 19, 31, 37 and 38. She held that the "claim for use in claim 12 is limited by the reference in claim 1 to the reduction of intraocular pressure 'without causing substantial ocular irritation'" (reasons at para. 62). She construed claim 19 as a compound *per se* claim and claims 31, 37 and 38 as claims for the use of the compound in claim 19 (reasons at paras. 60, 63-68).

[15] Turning to the issue of anticipation, the Applications Judge identified the approach adopted by Rothstein J. in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, [2008] 3 S.C.R. 265, as being applicable. She reviewed a number of documents, including Canadian Patent No. 986,926 (the '926 Patent), and found that none of them disclosed the chemical composition of latanoprost as defined in the '132 Patent (reasons at para. 95).

[16] With respect to utility, the Applications Judge found that the '132 Patent demonstrates utility. The test results on animals and humans disclosed in the patent show that latanoprost reduces intraocular pressure with minimal irritative side effects (reasons at paras. 143, 145).

[17] Even though she found that utility had been demonstrated, the Applications Judge briefly addressed the issue of sound prediction. She identified the three elements of the doctrine of sound prediction set out by Binnie J. in *Apotex Inc. v. Wellcome Foundation Ltd.*, [2002] 4 S.C.R. 153 at para. 70, ***i.e.*** there must be a factual basis for the prediction; the inventor must have as of the date of the patent application a sound line of reasoning from which the desired result can be inferred from the factual basis; and there must be proper disclosure. The Applications Judge held that the evidence adduced by the respondents supported a finding of sound prediction (reasons at para. 154).

ALLEGED ERRORS

[18] At the hearing of the appeal, counsel for the appellant advised that she was no longer pursuing the argument that the '132 Patent was invalid as a selection patent but that she was pursuing the remaining five arguments set out in her memorandum of fact and law.

[19] The first is that the Applications Judge failed to construe claim 12 and in particular the phrase "substantial ocular irritation" found in claim 1, on which claim 12 depends. The appellant submits that had she construed those words, "it would have been clear that latanoprost was not better than the prior art $PGF_{2\alpha}$-isopropyl ester since neither compound resulted in patients discontinuing therapy in the reported clinical studies" (appellant's memorandum at para. 35).

[20] Second, the appellant submits that the Applications Judge erred in her assessment of anticipation in relation to claim 19, a compound *per se* claim. It contends that the Applications Judge erroneously required that the prior art disclose the use of the compound in treating glaucoma. Furthermore, the appellant submits that the '926 Patent discloses the chemical structure of latanoprost acid and the method of making it. As such, there is both disclosure and enablement, and the Applications Judge erred in failing to find that claim 19 was anticipated.

[21] Third, the appellant submits that all the claims in issue lack utility and that the Applications Judge's failure to so find is due to her improper application of the relevant test. It argues that the '132 Patent does not demonstrate the promised utility, *i.e.* that latanoprost is a therapeutically more useful compound than the known intraocular pressure-lowering prostaglandins and does not cause substantial ocular irritation.

[22] The appellant further submits that the Applications Judge failed to correctly apply the test for sound prediction. It contends that there was no factual basis for the prediction, that the testing involving cats was not predictive, and that the limited human testing was insufficient to predict that the general population would not suffer from ocular irritation. Furthermore, the appellant argues that there is no disclosure of human data or head to head testing against the known $PGF_{2\alpha}$-isopropyl ester to support the claim of less irritation.

[23] Finally, the appellant submits that the Applications Judge failed to consider that claims 19, 31, 37 and 38 are broader than the invention made or disclosed.

ANALYSIS

[24] Before turning to the analysis, it is useful to recall that errors of law are reviewable on a standard of correctness and that factual findings will not be altered unless the Applications Judge committed a palpable and overriding error (*Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R. 235).

[25] The first error alleged is that the Applications Judge failed to properly construe claim 12 of the '132 Patent because she made no finding as to the meaning of the phrase "substantial ocular irritation" in claim 1 on which it depends. It is true that the Applications Judge in construing the '132 Patent did not specifically address this phrase. However, when addressing the issue of utility, she stated that "substantial ocular irritation" in claim 12 "does not refer to the elimination of all side effects", thereby rejecting the position adopted by the appellant as outlined in the affidavit of Dr. Mitra, one of its experts (reasons at para. 142).

[26] The appellant on appeal does not take issue with this finding. It now adopts the opinion expressed by Dr. Neufeld according to whom "substantial ocular irritation" means "a level of ocular irritation or ocular discomfort that would cause a patient to stop taking latanoprost" (appellant's memorandum at para. 6). This is consistent with the view expressed by the Applications Judge. Indeed, it is clear from a reading of the decision as a whole that the Applications Judge adopted the position of Dr. Neufeld with which the appellant now agrees. As such, no error can be said to result from the Applications Judge's reading of claim 12.

[27] The second error alleged is that the Applications Judge read a use limitation into claim 19 when assessing whether the claim was anticipated even though she construed claim 19 as a compound *per se* claim. The appellant further submits that the chemical structure of "latanoprost acid" and the method for making it were disclosed in the '926 Patent. It also submits that the '926 Patent discloses that the invention can be esterified to make alkyl esters, of which isopropyl is one. The appellant thus contends that the invention claimed in the '132 Patent was disclosed and enabled, and therefore anticipated.

[28] The Applications Judge made it clear that claim 19 claims a compound *per se* (reasons at para. 58). However, the appellant focuses on a phrase in her anticipation analysis which suggests that latanoprost is a chemical composition "for the treatment of glaucoma or ocular hypertension" (reasons at para. 95). As the appellant properly points out, it is claims 31, 37 and 38 that claim this specific use for the compound in claim 19.

[29] However, this does not alter the Applications Judge's conclusion that the compound claimed in the '926 Patent is not the same as the compound claimed in claim 19 of the '132 Patent. The Applications Judge's finding is supported by the evidence. It shows that latanoprost acid is distinct from latanoprost. In his affidavit, Dr. Maxey stated the following (affidavit, appeal book, vol. 2 at p. 601):

> 43. In order to call a molecule the "latanoprost free acid" or the "methyl ester of latanoprost" as Dr. Mitra does, or "the optically active methyl ester of the 13,14-unsaturated version of latanoprost" as Dr. Prestwich does, one needs to already know the structure of latanoprost, which is 13,14-dihydro-17-phenyl-18,19,20-trinor $PGF_{2\alpha}$ isopropyl ester. Put another way, one can only call these molecules

> 'latanoprost' free acid or 'latanoprost' methyl ester or "the optically active methyl ester of the 13,14-unsaturated version of latanoprost" with hindsight. Neither Dr. Mitra nor Dr. Prestwich opine that 13,14-dihydro-17-phenyl-18,19,20-trinor $PGF_{2\alpha}$ isopropyl ester (latanoprost) was previously known.
>
> …
>
> 48. Similarly, Canadian Patent 986,926 (PMS Document #25) does not disclose latanoprost. Dr. Mitra states that latanoprost "as an acid and as an alkyl ester (which would include isopropyl ester)" is disclosed. My discussion at paragraph 43 is equally applicable here. I see no discussion in Document #25 that teaches the compound 13,14-dihydro-17-phenyl-18,19,20-trinor $PGF_{2\alpha}$ isopropyl ester.
>
> [Footnote omitted]

[30] Dr. Neufeld opined in the same direction (affidavit, appeal book, vol. 3 at p. 772):

> 43. Amongst the numerous compounds disclosed in Canadian Patent No. 986,926, I cannot find 13,14-dihydro-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$-IE, now known as latanoprost. Furthermore, none of the molecules that are disclosed in Canadian Patent No. 986, 926 are for ophthalmic use. The "therapeutic" use for the thousands of compounds disclosed in Canadian Patent No. 986,926 is induction of labour or control of the oestrus cycle, which relates to the reproductive cycle. Nothing about these uses would lead one skilled in the art to an ophthalmic use, such as treating glaucoma or ocular hypertension.
>
> 44. In paragraph 49 of his affidavit, Dr. Mitra states that "… latanoprost, as an acid and as an alkyl ester …" was disclosed in Canadian Patent No. 986,926 as a "therapeutic compound". Latanoprost does not exist as an acid nor is it an unspecified alkyl ester. Latanoprost is 13,14-dihydro-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$-IE. This coumpound is nowhere disclosed in this patent.
>
> [Emphasis added]

[31] Based on the evidence before her, it was open to the Applications Judge to find that latanoprost was not anticipated by the '926 Patent.

[32] The third alleged error relates to utility. The appellant submits that the promise of the patent – that latanoprost is a therapeutically more useful compound that the known intraocular pressure-lowering prostaglandins as it does not cause substantial ocular irritation as did the prior art compound – has not been demonstrated. Specifically, the Applications Judge erred in finding that "[l]atanoprost will be useful in the treatment of ocular hypertension or glaucoma", because the promise of the '132 Patent is that latanoprost is more useful than the prior known compound.

[33] However, the conclusion reached by the Applications Judge is that latanoprost had less side effects that the prior known compound. Indeed, in her discussion relating to obviousness, the Applications Judge stated that she preferred the evidence of Dr. Neufeld and specifically referred to paragraph 46 of his affidavit, which states (reasons at para. 107):

> Dr. Johan W. Stjernschantz and Dr. Bahram Resul, who were working for Pharmacia, invented a new compound, latanoprost (13,14-dihydro-17-phenyl-18,19,20-trinor-$PGF_{2\alpha}$-IE), a compound useful for the treatment of patients with glaucoma or ocular hypertension. This compound had a better side effect profile than $PGF_{2\alpha}$-IE, i.e. a compound that had been previously tested in humans (see Document No. 127). Latanoprost was shown to cause less ocular irritation and hyperemia.
>
> [Emphasis added]

[34] Furthermore, the Applications Judge stated that the '132 Patent "itself shows utility" (reasons at para. 143). She referred to pages 25 to 29 of the '132 Patent, which disclose test results from three animal models (cat, rabbit and monkey) and one human model. In each of the animal models (Tables III, IV and V in the '132 Patent), latanoprost and $PGF_{2\alpha}$-ispropyl ester were tested

and the results demonstrate that latanoprost causes no ocular irritation (Table III) and less hyperemia than $PGF_{2\alpha}$-isopropyl ester (Table IV).

[35] The appellant correctly points out that the Applications Judge also referred to page 22d of the '132 Patent as disclosing test results on latanoprost. The results contained on page 22d do not pertain to latanoprost. However, the error is immaterial as there was ample evidence – including pages 25 to 29 of the '132 Patent – by reference to which the Applications Judge could find that utility had been demonstrated.

[36] There is no basis for the appellant's further argument that the human testing involving Pharmacia employees who attested to the fact that latanoprost did not cause substantial ocular irritation should be discarded because they had "a vested interest in the outcome" (memorandum of the appellant at para. 14). The contention that these individuals had an interest in effectively misleading their employer as to the results of the testing is not rationally defensible.

[37] The fourth error alleged by the appellant is that the Applications Judge failed to correctly apply the test for sound prediction as there was no factual basis for the prediction. In light of my conclusion that the Applications Judge properly found that there was utility, there is no need to address the appellant's submission on sound prediction. Nevertheless, I am satisfied that the evidence supports her alternative view that the invention was soundly predicted.

[38] The final error is that the Applications Judge failed to find that claims 19, 31, 37 and 38 are broader than the invention made or disclosed. This seems to be a new argument. The argument at trial, which was addressed by the Applications Judge in her reasons, was that the claims at issue failed for overbreath because they did not claim a reduction in hyperemia (reasons at para. 159).

[39] The novel issue raised on appeal is that the Applications Judge failed to compare the invention disclosed to the claims (appellant's memorandum at para. 54). The theory behind this argument appears to be that the claim must mirror the disclosure of the patent. No authority has been cited for this proposition.

[40] The Applications Judge referred to *Lowell Manufacturing Co. and Maxwell Ltd. v. Beatty Bros. Ltd.* (1962), 41 C.P.R. 18 (Ex. Ct.) for the proposition that (reasons at para. 156):

> [i]f the claims read fairly on what has been disclosed and illustrated in the specification and drawing, …, they are not wider than the invention …

[41] This statement was endorsed by this Court in *Pfizer Canada Inc. v. Minister of Health*, 2007 FCA 209, wherein it made clear that a claim will be considered overbroad if it asserts a right of exclusive property in something which the inventor did not actually invent or disclose. No such issue arises here.

[42] It has not been shown that the Applications Judge erred in failing to find that the claims are broader than the invention.

[43] I would dismiss the appeal with costs.

"Marc Noël"

J.A.

"I agree
Johanne Trudel J.A."

"I agree
Robert M. Mainville J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-22-10
(APPEAL FROM A JUDGMENT OF THE HONOURABLE MADAM JUSTICE HENEGHAN DATED DECEMBER 18, 2009, DOCKET NO. T-2221-07.)	
STYLE OF CAUSE:	Pharmascience Inc. v. Pfizer Canada Inc. and Pharmacia Atkiebolag and The Minister of Health
PLACE OF HEARING:	Montréal, Quebec
DATE OF HEARING:	February 23, 2011
REASONS FOR JUDGMENT BY:	Noël J.A.
CONCURRED IN BY:	Trudel J.A. Mainville J.A.
DATED:	March 17, 2011

APPEARANCES:

Carol Hitchman Arif Mahmood	FOR THE APPELLANT
Brian Daley Kavita Ramamoorthy	FOR THE RESPONDENTS

SOLICITORS OF RECORD:

GARDINER ROBERTS LLP Toronto (Ontario)	FOR THE APPELLANT
OGILVY RENAULT LLP Montréal, Quebec	FOR THE RESPONDENTS