Federal Court of Appeal | Cour d'appel fédérale

Date: 20110816

Docket: A-206-10

Citation: 2011 FCA 236

CORAM: **SHARLOW J.A.**
TRUDEL J.A.
STRATAS J.A.

BETWEEN:

APOTEX INC.

Appellant

and

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

Respondents

Heard at Toronto, Ontario, on June 20, 2011.

Judgment delivered at Ottawa, Ontario, on August 16, 2011.

REASONS FOR JUDGMENT BY: TRUDEL J.A.

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

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REASONS FOR JUDGMENT

TRUDEL J.A.

Introduction

[1] The question on this appeal turns on whether Heneghan J. of the Federal Court (the Applications Judge) erred in her construction of Canadian Patent 1,339,132 (the '132 patent or Patent '132 or the patent).

[2] In a judgment dated April 26, 2010 (2010 FC 447), the Applications Judge granted Pfizer Canada Inc. and Pharmacia Atkiebolag (together Pfizer) an order prohibiting the Minister of Health from issuing a Notice of Compliance to Apotex Inc. (Apotex), pursuant to section C.08.004 of the *Food and Drug Regulations*, C.R.C., c. 870, until the expiry of the '132 patent in 2014.

[3] The '132 patent claims, *inter alia*, a compound known as latanoprost used in the treatment of glaucoma and ocular hypertension. Latanoprost, in the form of a 50 microgram/ml ophthalmic solution, is sold in Canada under the name of Xalatan®.

[4] Apotex served its Notice of Allegation (NOA) on Pfizer on March 4, 2008, alleging that each of the claims of the '132 patent was invalid on the following grounds: double patenting, lack of novelty and inventiveness, including anticipation and obviousness, overbreadth and inutility. Moreover, Apotex asserted that its generic version of Xalatan®, Apo-Latanoprost, would not infringe Patent '132 under the Gillette defence doctrine (appeal book, volume 1, tab 3, at page 69). Finally, Apotex argued that Patent '132 did not meet the conditions for a valid selection patent (*ibidem*, at pages 140 and following). At the hearing of this appeal, all these grounds remained, except for overbreadth and inutility, which were no longer pursued by Apotex.

[5] I need not address all these grounds of invalidity. I agree with Apotex that the Applications Judge erred in her construction of the promise of the '132 patent, an error which affected the rest of her analysis. As a result, she never fully considered whether the promised utility was soundly predicted. Having considered the patent's factual basis and the evidence as a whole, I conclude that

the ‘132 patent fails to meet the requirements for sound prediction. Therefore, I would allow this appeal for the reasons that follow.

The Patent

[6] The ‘132 patent, entitled “Prostaglandin Derivatives for the Treatment of Glaucoma or Ocular Hypertension” was filed on September 12, 1989. As such, it falls under the purview of the *Patent Act*, R.S.C. 1985, c. P-4 (the Act), as it read prior to October 1, 1989. The patent was issued on July 29, 1997 and will expire on July 29, 2014.

[7] The patent addresses certain prostaglandin derivatives and their use in the treatment of glaucoma or ocular hypertension. 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 for judgment, at paragraph 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. 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.

Glaucoma, Ocular Hypertension and Latanoprost

[9] 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 not only conveys nutrients to it, but also removes from it waste products and contaminants. The drainage of aqueous humor assists in avoiding an increase in intraocular pressure, thus reducing the risk factor for disorders of the eye, including glaucoma and ocular hypertension.

[10] Ocular hypertension describes an intraocular hypertension without damage to the optic nerve. Glaucoma describes a group of disorders characterized by damage to the optic nerve that results in loss of vision if the condition is left untreated. There is no cure for glaucoma but it, as well as ocular hypertension, can be managed by reducing intraocular pressure. This is achieved by use of drugs in one of two ways: reduction in the production of aqueous humor; or, with latanoprost, increase in the outflow of aqueous humor.

[11] A high level of compliance is needed by patients treating their glaucoma with drugs. Therapies with less frequent doses are preferred because they contribute to patients' compliance, as does the tolerability of the drugs used. The tolerability of the drug is usually measured in terms of side effects, which may be systemic (occurring throughout the body) or localized (around the eye).

[12] Prior to the advent of latanoprost, other drugs were available for the treatment of glaucoma and ocular hypertension. They, however, caused undesirable effects, ranging from tingling and

hyperaemia to emphysema and death. Latanoprost was claimed to "reduce intraocular pressure without causing substantial ocular irritation" (claim 1 of the '132 patent).

[13] According to Apotex, this claimed utility, correctly construed, means that chronic use of latanoprost will "reduce intraocular pressure without causing substantial ocular irritation": glaucoma is a chronic disease, the management of which requires chronic treatment.

[14] The gist of Apotex's argument is that at the time of the filing of the '132 patent, the inventors had only conducted single dose studies, yet promising that the compounds can be used chronically without eliciting unwanted side effects. As a result, Apotex argues that the '132 patent is not based on demonstrated utility, but rather on a prediction of chronic treatment without substantial side effects. Because the '132 patent fails to disclose a sound line of reasoning to bridge the gap between the factual basis of the patent (the one dose studies) and its promise, it must fail. This is the pivot of Apotex's arguments.

[15] The Applications Judge went on to methodically examine the parties' arguments and all the invalidity grounds raised by Apotex. In view of my conclusion above and for ease of reference, I will only refer to the relevant part of her reasons in my analysis.

Standard of Review and *De Novo* Determination

[16] This appeal is mostly concerned with the construction of the claims of the '132 patent. As claims construction is a matter of law, the standard of review is that of correctness (*Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, [2000] 2 S.C.R. 1067, at paragraph 61 [*Whirlpool*]; *Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R. 235, at paragraph 8).

[17] Like claims construction, the promise of the patent is also a question of law (*Eli Lilly Canada Inc. v. Novopharm Ltd.*, 2010 FCA 197 [*Eli Lilly*]). In this particular case, the Applications Judge, assisted with expert evidence, needed to purposively ascertain the promise of the patent "within the context of the patent as a whole, through the eyes of the person of skill in the art (POSITA) in relation to the science and information available at the time of filing" (*Eli Lilly*, at paragraph 80).

[18] In view of my conclusion that the patent is not based on demonstrated utility, it becomes necessary to determine whether the promised utility of the '132 patent was soundly predicted. Soundness of the prediction is a question of fact (*Apotex Inc. v. Wellcome Foundation Ltd.*, 2002 SCC 77, [2002] 4 S.C.R. 153, at paragraph 71 [*Wellcome AZT*]). Absent an overriding and palpable error, the Applications Judge's conclusion shall not be disturbed.

[19] Here, having dismissed the "chronic use" construction advanced by Apotex, the Applications Judge rapidly addressed and dismissed Apotex's ensuing argument about the

unsoundness of the patent (reasons for judgment, at paragraphs 179 to 186), because in her view, Apotex's argument was unsupported by its own expert evidence (*ibidem*, at paragraph 185). I respectfully disagree. I find that there was strong and convincing evidence on record supporting Apotex's claim for lack of sound prediction.

[20] As a result, this Court will have to make some findings of fact. Following the methodology adopted by Rothstein J. in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, [2008] 3 S.C.R. 265, at paragraph 72 [*Sanofi*], and because the record is complete and the parties have fully argued the point before us and below, I propose to examine Apotex's argument *de novo* rather than remit the matter to the Applications Judge for redetermination.

Analysis

A. Claims Construction

[21] After setting up the background of the proceeding, the Applications Judge construed the patent at paragraphs 64 to 83 of her reasons. As already mentioned, the parties were agreed that only claims 12, 19, 31, 37 and 38 were relevant to the disposition of Pfizer's application. The Applications Judge found no compelling reason not to construe the claims as she had done in a previous case (*Pfizer Canada Inc. v. Canada (Minister of Health)*, 2009 FC 1294; aff'd 2011 FCA 102). Pfizer notes correctly that the construction of the '132 patent, as stated by the Applications Judge in the previous proceeding, was upheld on appeal.

[22] However, it does not follow that Apotex, which was not a party to the previous proceeding, is precluded in this case from asserting a different construction of the patent based on an issue that was not previously raised. Pfizer does not say that the point of patent construction raised by Apotex in this case was in issue in the previous case. Indeed, it is not clear from the reasons of the Applications Judge in the previous case whether the construction of the '132 patent was in dispute at all between the parties. In the appeal of the previous case, there was a challenge to the correctness of the construction adopted by the Applications Judge. The issue was whether she failed to 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 depended. That point is not in dispute in the present application.

[23] Coming back to the Applications Judge's construction of the patent, with the teachings of the Supreme Court of Canada in *Free World Trust v. Électro Santé Inc.*, 2000 SCC 66, [2000] 2 S.C.R. 1024 in mind, she held that claim 19 is a compound *per se* claim while claims 31, 37 and 38 are claims for the use of the compound in claim 19. She also held that claim 12 is limited by the reference in claim 1 to the reduction of intraocular pressure "without causing substantial ocular irritation" (reasons for judgment, at paragraphs 74 to 82). Apotex does not attack the Applications Judge's approach to claims construction nor the legal principles she referred to or applied.

[24] For the Applications Judge, Apotex's position that the promise of the patent is chronic use of the compound amounted to a "mistaken premise" upon which Apotex wrongly relied for its case.

At paragraph 192 of her reasons, she held that Apotex "was unable to show that its basic premise was sound" and dismissed the argument. I agree with Apotex that, in so doing, the Applications Judge overlooked Pfizer's own evidence that glaucoma, at the time of filing, would have been known by the POSITA to be a chronic condition that required chronic treatment.

[25] Dr. Fechtner, expert for Pfizer, conceded that when speaking of treatment of glaucoma, the POSITA would know that one is referring to chronic use (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1086). When asked whether the claims 37 and 38 of the patent would contemplate chronic treatment, he answered: "For me, implicit in treatment of glaucoma or ocular hypertension is chronic treatment" (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1086). Dr. Stjernschantz, one of the two inventors of the patent, concurred that glaucoma, perhaps with the exception of acute glaucoma, was a chronic disease. He and two other experts for Pfizer also agreed that the use of a topical treatment to treat glaucoma requires chronic use (cross-examination of Dr. Stjernschantz, appeal book, volume 3, tab 3, at page 1147; cross-examination of Dr. Neufeld, appeal book, volume 3, tab 54, at page 1196; cross-examination of Dr. Wolff, appeal book, volume 3, tab 55, at page 1240).

[26] Pfizer disagrees with this proposed construction which, in its opinion, confuses claim construction with medical treatment of a disease. For Pfizer, the fact that a disease requires long term treatment is a matter for physicians and not for this Court tasked with the determination of claims construction (respondent's memorandum, at paragraph 50). At the hearing, Pfizer

emphasized that adopting Apotex's construction would amount to "reading in" a chronic element into the claims.

[27] I disagree. The POSITA was defined by the Applications Judge as "a medicinal or organic chemist or a pharmacologist, holding at least a Bachelor's degree, with some familiarity with prostaglandins and the ophthalmological field, as well as a medical doctor specializing in ophthalmology" (reasons for judgment, at paragraph 137). Defined as such, there is uncontested evidence that the POSITA would have known that glaucoma is a chronic disease. I see it as an error to construe the promise of the '132 patent without consideration as to the nature of the disease it purports to treat effectively. This conclusion was expressly drawn by Dr. Fechtner (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1089):

> Q. But do you realize – we've discussed this already – the compounds being analyzed in this patent were intended to be used <u>chronically</u>?
>
> A. <u>That is the promise of the patent.</u>

[28] In my view, the Applications Judge erred in law in failing to consider the evidence as a whole in her construction of the promise of the patent. Had she done so, she would have found that the patent fails for lack of sound prediction.

B. Non-Demonstrated Utility

[29] Relying on several findings of fact, the Applications Judge held that the patent demonstrated utility as of September 12, 1989 (reasons for judgment, at paragraphs 167 to 175). Having dismissed Apotex's chronic use argument, her findings were informed by her previous construction that the promise of the patent did not include chronic treatment. As I disagree with the Applications Judge on this point, I will look at the issue of demonstrated utility and sound prediction from the perspective that the promise of the patent is chronic use of the compound for a chronic medical condition.

[30] Section 2 of the Act requires that the subject matter of a patent be new and useful. The granting of a patent is dependant upon the disclosure of how the patent intends to fulfill its promise (*Pfizer Canada Inc. v. Canada (Minister of Health)*, 2008 FCA 108, [2009] 1 F.C.R. 253, at paragraph 34; *Wellcome AZT*, at paragraph 66). The general principle is that, as of the date of the filing, a patent must disclose either an actually achieved result (i.e., prove that it does what it claims) or a basis for sound prediction of the result (i.e., show that it is likely to do what it claims). There is no requirement to prove demonstrated utility in the disclosure of the patent; so long as the disclosure makes reference to a study demonstrating that the patent does what it promises to do, this criteria is met (*Pfizer Canada Inc. v. Novopharm Ltd*., 2010 FCA 242, at paragraph 90). In our case, utility would be demonstrated if the patent disclosed studies showing that latanoprost, when administered on a chronic basis, reduced intraocular pressure without causing substantial side effects.

[31] However, at the time of filing, the uncontested evidence was to the effect that the inventors had only conducted "single dose" studies on animals and healthy humans; latanoprost had not been tested on patients with glaucoma or on a chronic basis. The evidence from experts on both sides also reveals that the '132 patent was based on a prediction of utility, *i.e.*, that which was observed in the single dose study could soundly be predicted to apply to chronic use (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1091; cross-examination of Dr. Wolff, appeal book, volume 3, tab 55, at pages 1240 and 1242; Leibowitz's affidavit, appeal book, volume 8, tab 69, at page 3321). Dr. Stjernschantz confirmed that, at the time of filing, the utility of the patent was not demonstrated (cross-examination of Dr. Stjernschantz, appeal book, volume 3, tab 53, at pages 1149 and 1154):

> Q. I understand. And by the time of this patent's filing, which – take my word for it – is September 1989, you had not tested any of the compounds in the invention so as to demonstrate that the compounds could treat chronic glaucoma without side effects in humans?
>
> A. We had not tested any of the drugs in patients suffering from glaucoma.
>
> Q. Right. And in so far as the patent claim claims the treatment of people who had, as an ailment, glaucoma, it was a prediction?
>
> A. Yes. It was a prediction yes.

[32] The evidence leads me to the conclusion that the utility of the '132 patent, as of its filing date, is based not on a demonstration of utility but on a prediction. The question that must now be

answered is whether this prediction is a sound one. I agree with Apotex that the patent fails for not meeting the test for sound prediction.

C. Sound Prediction

[33] The doctrine of sound prediction seeks to balance two competing public interests: the desirable early disclosure of new and useful inventions, even though their utility has not been fully verified by tests, and the need to ensure that patent rights are not granted in exchange for misinformation (*Sanofi*, at paragraph 105; *Wellcome AZT*, at paragraph 66). Thus, if a patentee can articulate a sound prediction as to the utility of his invention, he should be entitled to base a claim on it. And although patents shall not be granted in exchange for misinformation, mere speculation or lucky guesses, a sound prediction does not amount to certainty (*Wellcome AZT*, at paragraph 69; *Monsanto Co. v. Canada (Commissioner of Patents)*, [1979] 2 S.C.R. 1108, at page 8).

[34] The doctrine of sound prediction has three components, as listed in *Wellcome AZT* (at paragraph 70). All must be met for a patent to survive the test:

1) There must be factual underpinnings for the prediction;

2) There must be an articulable and "sound" line of reasoning from which the desired result can be inferred from the factual basis; and

3) There must be proper disclosure.

[35] I will first deal with the Applications Judge's finding that Apotex did not meet its evidentiary burden as to the gap between the factual basis and the promise of the patent (the "gap issue"). She dismissed Apotex's argument as follows (reasons for judgment, at paragraph 185):

> At the hearing, the Respondent alleged that the '132 patent failed to address the gap between the single dose studies found within the patent and the fact that the treatment of glaucoma or ocular hypertension requires chronic use of medication, i.e., long-term and usually life-time treatments. None of the Respondent's expert made reference to this in their affidavits nor did they address this factor when speaking about the NOA prior art.

[36] However, Dr. Leibowitz, expert for Apotex, precisely addressed the gap issue in his affidavit (appeal book, volume 8, tab 69, at page 3325):

> Further, the use of single dose observations is at odds with the expected daily lifetime use of the compound. Data derived only from a single dose does not establish a lack of irritating effect of a compound designed for repeated and prolonged use.

[37] Moreover, the gap issue was also addressed by Pfizer's experts (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1082; cross-examination of Dr. Wolff, appeal book, volume 3, tab 55, at page 1241; cross-examination of Dr. Stjernschantz, appeal book, volume 3, tab 53, at page 1154). There was, therefore, evidence on both sides on the gap issue. The fact that

the Applications Judge ignored or overlooked this evidence certainly cut short her analysis of sound prediction.

[38] I will now turn to the test for sound prediction. The first element of the analysis for sound prediction is whether there is a factual basis supporting the patent's prediction. It bears repetition that the promise of the patent was to treat glaucoma and intraocular hypertension on a chronic basis without causing substantial side effects.

[39] The '132 patent discloses studies that tested a number of prostaglandins derivatives for topical use in the lowering of intraocular pressure. The studies consisted of putting a single dose of the compounds in the eye of the animal and human models. The tests were broken down so that the efficacy of the compounds was tested in monkeys and humans, whereas toxicity (irritation and hyperaemia) was tested in rabbit and cat models (tables 3 to 6 of the 132 patent; cross-examination of Dr. Stjernschantz, volume 3, tab 53, at pages 1150 and following).

[40] However, the factual basis supporting the promise of the patent is clearly not a chronic use study. None of the studies used multiple doses, as confirmed by Dr. Neufeld (appeal book, volume 3, tab 54, at page 1197):

> Q. Okay, but the studies in the patent that have been included are not chronic studies.
>
> A. Correct.

> Q. And they are all – all of them are one-time uses of the medicines?
>
> A. Yes.
>
> (*See also* cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1088.)

[41] I will now turn to the second element of the test for sound prediction, i.e., whether there is an articulable and sound line of reasoning between the factual basis and the patent's promise.

[42] The inventor's line of reasoning is nowhere to be found in the disclosure of the '132 patent. When asked where, in the patent, was disclosed the line of reasoning, Dr. Wolff could not point to any excerpt (cross-examination of Dr. Wolff, volume 3, tab 55, at page 1243). Dr. Fechtner's was led to the same conclusion (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1091):

> Q. Yes. So can you point me in the patent where the inventor say here's the rational from Point A, one time single use, the tables, to Point B, lifelong chronic use, the claims? Where's the description of that rational in the patent?
>
> […]
>
> A. I don't find explicitly what you're describing.

[43] At the hearing, counsel for Pfizer argued that the line of reasoning was to be found in the studies listed in the "References" section of the patent (Patent '132, at pages 30 and 31). Pfizer also

took the position that a POSITA, taking the prior art as a whole, would be able to infer that multiple doses of latanoprost would give the same results as the single dose studies.

[44] This position seems at odds with the concept of disclosure in patent law. In *Wellcome AZT*, Justice Binnie stated that if utility is not demonstrated at the time of filing, the *quid pro quo* the applicant offers in exchange for the patent monopoly is a sound prediction of utility (*Welcome AZT*, at paragraph 70). As the applicant is the one who will benefit from the monopoly, I am of the view that only he, and not the authors or inventors of the prior art, can discharge himself of the obligation of disclosure. Besides, our Court found in *Eli Lilly Canada Inc. v. Apotex Inc.*, 2009 FCA 97, at paragraph 17 that a patent that provides no more disclosure than is available in the prior art does not provide a sound basis for the prediction.

[45] Moreover, Pfizer pointed to no evidence on the record supporting its position. None of Pfizer's experts bridged the gap between the single doses studies and the claimed chronic use. Dr. Stjernschantz and Dr. Fechtner limited their comments to the suitability of cat and rabbit models to test toxicity – the cat eye is more sensitive than the human eye, which makes it a good model for predicting ocular discomfort; the rabbit eye has a pronounced tendency to hyperaemic reactions and makes it a sound model for screening drugs for hyperaemic solution – and the suitability of monkey models to predict intraocular pressure in human – their eyes are anatomically and physiologically similar to the human eye (affidavit of Dr. Stjernschantz, volume 2, tab 40, at page 879; affidavit of Dr. Fechtner, volume 1, tab 10, at page 381; affidavit of Dr. Neufeld, appeal book, volume 2, tab 39, at page 831).

[46] Dr. Wolff also discussed the line of reasoning between tests conducted on healthy patients and predictions in glaucomatous patients (affidavit of Dr. Wolff, appeal book, volume 3, tab 46, at page 969). Pfizer pointed to none of its experts explaining how and why single dose studies could provide a sound basis for the prediction that latanoprost, used on a chronic basis, would treat glaucoma and ocular hypertension without substantial side effects.

[47] There is substantial evidence, however, showing that single dose studies may not predict long-term effects of a compound. Dr. Leibowitz, cited at paragraph 35 *supra*., affirmed that data derived only from a single dose does not establish a lack of irritating effect of a compound designed for repeated and prolonged use. His view is supported by the prior art, an excerpt of which reads (appeal book, volume 5, tab 64(35), at page 2288):

> When 0.5 μg $PGF_{2\alpha}$ was given twice daily for two weeks there was a tendency towards increasing discomfort during the study. Although the discomfort was mild even at the end of the study, this observation suggests that side effects may increase with repeated treatment.

[48] Even Pfizer's experts expressed doubts that a sound prediction existed. Dr. Wolff cautioned that results obtained for a single dose may change under chronic administration (cross-examination of Dr. Wolff, appeal book, volume 3, tab 55, at page 1241). Dr. Fechtner, who was of the same opinion, said (cross-examination of Dr. Fechtner, appeal book, volume 3, tab 50, at page 1089):

> Q. And you'd agree that the onset of adverse effects may not manifest itself after a single administration. Is that fair?
>
> A. I would agree with that.

[49] In light of the record as a whole, I have not been persuaded by Pfizer that the inventors had, at the time of filing, an articulable and sound line of reasoning bridging the gap between the factual basis and the promise of the patent. Therefore, I conclude that the patent does not meet the second prong of the test for sound prediction.

[50] I am mindful of Pfizer's position that Apotex's gap argument could mean that only long term testing in diseased humans would satisfy the test for sound prediction (respondent's memorandum, at paragraph 102). It seems to me, however, that the information required for sound prediction is case specific and needs to be established in light of the evidence. Suffice it to conclude that in the present case, the evidence was insufficient to soundly predict that latanoprost would fulfill its promise.

[51] I will now turn to the third element of the test for sound prediction: proper disclosure. When examining this element, the Court must determine whether the specification provides a full, clear and exact description of the nature of the invention and the manner in which it can be practised (*Wellcome AZT,* at paragraph 70). Of course, the disclosure requirement rests on the first two requirements of the test for sound prediction.

[52] The amount of disclosure required to meet the third prong of the test for sound prediction has been discussed in *Eli Lilly Canada Inc. v. Apotex Inc*., 2008 FC 142; aff'd on this point in 2009 FCA 97. Justice Noël, writing in appeal, held that when a patent is based on a sound prediction, the disclosure must include the prediction (at paragraph 15). Most recently, our Court has held that "(w)hen utility is based on sound prediction, disclosure of its factual foundation goes to the essence of the bargain with the public underlying patentability" (*Eli Lilly and Company v. Teva Canada Limited*, 2011 FCA 220, at paragraph 51). Pfizer has not persuaded me that there is sufficient evidence, in the patent and on the record, to support its position.

[53] I conclude that Pfizer has not proven, on a balance of probabilities, that Apotex's allegation of lack of sound prediction was unjustified.

Conclusion

[54] The Applications Judge made an error in her construction of the promise of the patent which sent her down the wrong path. Had she properly construed the patent as promising treatment through chronic use of the compounds, she would have found it invalid for failing to make a sound prediction of utility. As such, I need not look at the other grounds of invalidity raised by Apotex. Pfizer's application for a prohibition order fails on this basis alone.

[55] For these reasons, I would allow the appeal and set aside the judgment of the Federal Court. Rendering the judgment which ought to have been rendered, I would dismiss the application. I would also allow Apotex its costs both in this Court and in the Federal Court.

"Johanne Trudel"
J.A.

“I agree
K. Sharlow J.A.”

“I agree
David Stratas J.A.”

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

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