Federal Court of Appeal | Cour d'appel fédérale

Date: 20110705

Docket: A-387-10

Citation: 2011 FCA 220

CORAM: **NOËL J.A.**
EVANS J.A.
DAWSON J.A.

BETWEEN:

ELI LILLY AND COMPANY

Appellant

and

TEVA CANADA LIMITED
(formerly known as NOVOPHARM LIMITED)

Respondent

Heard at Ottawa, Ontario, on June 22, 2011.

Judgment delivered at Ottawa, Ontario, on July 5, 2011.

REASONS FOR JUDGMENT BY: EVANS J.A.

CONCURRED IN BY: NOËL J.A.
DAWSON J.A.

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REASONS FOR JUDGMENT

EVANS J.A.

Introduction

[1] This is an appeal by Eli Lilly and Company (Lilly) from a decision of the Federal Court (2010 FC 915). In that decision, Justice Barnes (Judge) granted to Teva Canada Limited (Teva) a declaration under subsection 60(1) of the *Patent Act*, R.S.C. 1985, c. P-4, that Lilly's Canadian Patent No. 2,209,735 ('735 patent) was invalid for lack of utility. Teva was formerly Novopharm Limited and is referred to in the Judge's reasons as Novopharm.

[2] The subject of the patent is a new use for an old medicine that has long been in the public domain: atomoxetine for the treatment of three of the manifestations of attention deficit hyperactivity disorder (ADHD) for some people, regardless of their age group (adults, adolescents or children). ADHD is a neurobehavioral disorder, manifested by hyperactivity, inattention, and impulsiveness, and can impair functioning at school, work and in social settings. It is a chronic condition with no known cure, but its manifestations can be improved by medication.

[3] This appeal raises three principal legal issues. Did the Judge err by: (i) invalidating the ’735 patent for lack of demonstrated utility by misconstruing its promise; (ii) requiring too high a standard of proof of utility; and (iii) deciding that Lilly could not rely on the sound prediction of the utility of the invention because it had not disclosed the factual foundation of the sound prediction in the patent?

[4] The Judge approached the construction of the promise of the patent from the perspective of the relevant persons of skill in the art (POSITA), and concluded that the POSITA would understand the patent to promise clinically effective treatment of a chronic disorder, AHD.

[5] Having made findings of credibility of the principal experts and examined the documentary evidence, the Judge held that the study of the clinical trial on which Lilly relied was insufficient to demonstrate that atomoxetine would fulfil its promise. It was common ground that utility had to be demonstrated as of the date that Lilly filed its application for the ’735 patent, January 4, 1996.

[6] Finally, the Judge decided that he was bound by a decision of this Court holding that a claim of sound prediction can only succeed if the basis of the prediction is disclosed in the patent.

[7] In my view, the Judge's careful and thorough reasons reveal no reversible error.

[8] The principal dispute between the parties at trial was whether the single study on which Lilly relied was sufficient to demonstrate that atomoxetine was an effective treatment of ADHD for the purpose of establishing that it met the usefulness criterion of patentability in section 2 of the *Patent Act*. This is an essentially factual issue that turned on the Judge's assessment of the evidence which, in turn, depended in large part on his credibility findings. I am not persuaded that the Judge made any palpable and overriding error in his findings of fact or in his application of the law to the facts.

[9] On appeal, Lilly raised legal issues about the construction of the promise of the patent, the standard of proof required to demonstrate utility, and whether the factual basis for sound prediction must be disclosed in the patent. In my opinion, Lilly has not established that the Judge was wrong in his identification or formulation of the applicable law.

The MGH Study

[10] Lilly sponsored and funded a clinical trial that was conducted in 1995 at the Massachusetts General Hospital (MGH Study) on the effectiveness of atomoxetine in the treatment of ADHD. The

trial was described by Dr Heiligenstein, the inventor and a Lilly employee, as a pilot study designed to determine whether atomoxetine might be useful in treating ADHD.

[11] Twenty-one adult patients (half the number called for by the MGH study protocol) participated in the double-blind, placebo-controlled cross-over human clinical study. Half of the patients were given atomoxetine for three weeks, followed by a "wash-out" week, and a placebo for three weeks. The order was reversed for the other half of the patients. Neither the physicians nor the patients were informed whether atomoxetine or the placebo was being administered.

[12] Eleven of the patients showed a 30% or greater reduction in ADHD symptoms, whereas only two showed reduced symptoms after taking the placebo. These results met the predetermined standards set by the study's evaluators.

[13] The authors of a report on the MGH Study published in a prestigious medical journal stated that the results "confirm the study hypothesis and suggest that atomoxetine may be useful for the treatment of ADHD" (Appeal Book vol. 11, p. 4001). They also described them as "clinically and statistically significant", even though "the cross over design and the relatively short exposure may not have been ideal." They concluded:

> Although preliminary, these promising initial results provide support for further studies of tomoxetine [as atomoxetine was previously known] in the treatment of ADHD.

In the abstract of the report, they indicated that the further studies should be "over an extended period of time" (*ibid.* at p. 3999).

[14] On the basis of the MGH Study, Lilly set up a working group to examine three possible compounds for treating ADHD, including atomoxetine. Lilly selected atomoxetine for further development and obtained regulatory approval to market it in the United States in 2002 and in Canada in 2004.

Issues and analysis

(i) ***Standard of review***

[15] It was common ground that the Court may only reverse a decision of the Judge on the basis of his findings of fact or application of the law to the facts if he committed a palpable and overriding error. On questions of law, however, the Court may intervene if satisfied that the Judge was wrong.

[16] Lilly submitted that the Judge made four legal errors. First, he misconstrued the patent by implying a promise that atomoxetine was an effective *long term* treatment of ADHD. Second, he set the standard of proof of utility for patentability too high by failing to ask whether there was a scintilla of evidence of atomoxetine's usefulness in treating ADHD. Third, he reversed the onus of proof by requiring Lilly to prove utility, rather than putting the onus on Teva to prove lack of utility. Fourth, he held that Lilly could not establish utility on the basis of sound prediction because it had not disclosed in the patent the factual foundation of the prediction.

[17] Lilly did not directly take issue with the Judge's factual findings. However, counsel argued that, because the Judge had misconstrued the patent, he had reached the wrong conclusion on the basis of his findings of fact. He submitted that when the Judge's legal errors are corrected, it is clear

from the Judge's findings that Lilly had sufficient evidence to meet the low threshold needed to establish utility.

(ii) *Construction of the patent*

(a) implied promise

[18] The utility of the '735 patent must be determined by examining whether there was sufficient evidence demonstrating that, at the date of filing, atomoxetine would do what the patent promised or, if not, that its utility could be soundly predicted. Lilly says that the Judge erred in law by going beyond the promise expressly made in the patent and finding an implicit promise that atomoxetine "will work in the longer term" (at para. 112).

[19] I do not agree with Lilly's characterization of the Judge's reasons. The Judge's use of the phrase "implicit in the promise" (para. 112) must be considered in the context of the paragraph in which it appears.

> ADHD is a chronic disorder requiring sustained treatment. Only where experimental results are sufficiently compelling to independently support the inventive promise (or to support a sound prediction) is utility established. In the case of the '735 Patent, the inventors claimed a new use for atomoxetine to effectively treat humans with ADHD. What is implicit in this promise is that atomoxetine will work in the longer term. If the MGH Study was not adequate to demonstrate the clinical usefulness of atomoxetine to treat ADHD the bare fact that some positive experimental data emerged is not enough.

[20] In my view, Lilly's interpretation of this passage as a finding by the Judge of a second, implied promise in the patent is implausible. It assumes that the Judge forgot that he had previously construed the patent as promising that atomoxetine is an effective treatment for ADHD (at paras. 32,

79, and 93), a construction with which Lilly finds no fault. Indeed, the Judge concludes paragraph 112 by saying:

> The evidence to demonstrate utility must be sufficient to support the promise that atomoxetine works to treat ADHD in some patients.

[21] Only once does the Judge refer to long term effectiveness as implicit in the promise of the patent. In my view, when the Judge's reasons are read as a whole, he was not construing the patent as promising more than its explicit promise that it will treat ADHD in some people. Rather, he was simply interpreting what "treatment" means in this patent in the context of ADHD, a chronic disorder requiring sustained treatment. He was not adding a promise above and beyond that already expressed in the words of the patent, namely that atomoxetine is an effective treatment of ADHD.

(b) the meaning of "treatment"

[22] The parties agree that the patent promises that atomoxetine will treat, or effectively treat, some patients in all age groups by alleviating three manifestations of ADHD. It is equally uncontroversial that the patent is to be construed by examining it through the eyes of a POSITA and that the Judge was correct when he stated (at para. 7, note 2):

> The expert witnesses agreed that such a person would have a thorough knowledge of ADHD and its treatment and, in particular, the development, research or clinical use of ADHD drug therapies. I accept that this could include a psychiatrist, a paediatrician, doctorial pharmacist or a PhD in psychopharmacology.

[23] In my view, this definition of the qualifications of the POSITA relevant to this patent, and especially the inclusion of a psychiatrist and a paediatrician, indicates that he or she would interpret the promise from the perspective of a person involved in the clinical treatment of ADHD. A

POSITA would thus understand the promise to mean that atomoxetine will alleviate the symptoms of the disorder in some patients to a clinically meaningful extent. This is not to say that the promise means that clinicians will necessarily prescribe atomoxetine for their patients, because there may be more effective medicines available on the market. The promise does mean, however, that atomoxetine would be regarded by a physician as a realistic option for the treatment of ADHD.

[24] This conclusion is supported by the following exchange between counsel for Teva and Dr Kutcher, a psychiatrist**,** one of Teva's expert witnesses (Appeal Book, vol. 13, p. 4798):

> **Q.** When you read these claims what do they tell you, what are they talking about, the first, the use of tomoxetine [the previous name of atomoxetine] for treating ADHD disorder in a patient?
>
> **A**. That tells me that tomoxetine is something that could be used for treating a person that has ADHD.

[25] Similarly, when asked what he understood the promise of the patent to be, Dr Virani, a pharmacist specializing in psychopharmacology**,** the Teva expert witness whom the Judge found most credible, said (Appeal Book, vol. 14, p. 5025):

> … the promise here is that atomoxetine at reasonable and appropriate doses, would be a reasonable treatment strategy for alleviating the symptoms of ADHD, … in children, adolescents and adults.

[26] Lilly says that the Judge erred by interpreting the effective treatment promised in the patent as treatment that will continue to be effective in the long term. In my view, when his reasons are read as a whole, the Judge was not saying that, because ADHD has no known cure, the promise of effective treatment must mean that it will be effective as long as a patient is taking it, which could extend over a lifetime.

[27] On the other hand, when reading the promise a POSITA would have regard to the chronic nature of the disorder which the patent promises to treat effectively. For this reason, the Judge found as a fact that the clinical effectiveness of atomoxetine as a treatment must be "sustained" (at para. 112). This, in my view, is no more than a simple recognition of the fact that ADHD is not like a common headache, which can normally be effectively treated by one or two doses of a suitable medicine.

[28] Counsel for Lilly suggested that the manifestations of ADHD in some patients are sufficiently manageable that they only need medication for short periods at a time: to improve their level of concentration while preparing for and writing examinations, for example. Longer term effectiveness, it is argued, is not necessary to effectively treat these patients.

[29] In my view, this argument does not assist Lilly. The better reading of the Judge's reasons is that he found that the evidence was insufficient to demonstrate that atomoxetine was an effective clinical treatment, regardless of the length of time for which it was taken, and I see no basis for disturbing this conclusion. In any event, although the patent only promises that atomoxetine will treat *some* ADHD patients, there is no evidence that a POSITA would interpret the patent as limiting its promise of effective treatment to the relatively few ADHD patients who only need medication on a short term basis.

[30] Consequently, I am not persuaded that the Judge's interpretation of the patent was erroneous in law and undermined the conclusions that he drew from his findings of fact. In my view, the Judge

examined the evidence in light of the right question: when Lilly filed its application in 1996 for the ’735 patent, had it established that atomoxetine was a clinically effective treatment for ADHD for some patients?

(iii) ***Did Lilly have sufficient evidence that atomoxetine would effectively treat ADHD?***

[31] Counsel for Lilly argued that only a low level or scintilla of utility is required for the purpose of patentability: *Consolboard Inc. v. MacMillan Bloedel (Sask.) Ltd*., [1981] 1 S.C.R. 504 at 525, and *Aventis Pharma Inc. v. Apotex Inc*., 2005 FC 1283, 43 C.P.R. (4th) 161 at para. 271. The Judge erred in law, he submitted, by requiring evidence that is “sufficiently compelling to independently support the [patent’s] inventive promise” (at para. 112). This, counsel said, was a standard of proof more appropriate for obtaining regulatory approval which, as already noted, Lilly obtained in Canada on December 24, 2004, after extensive clinical trials.

[32] In my view, this argument cannot succeed in this case, because the patent specifically promised that atomoxetine is a clinically effective treatment of ADHD. The utility of the patent is thus determined by examining whether atomoxetine will do what Lilly promised that it would do. As the Judge put it (at para.112):

> I do not accept the point that utility in this case should be measured against a hypothetical or theoretical standard that is lower than the inventive promise of the patent.

[33] This issue was recently considered in *Novopharm Limited v. Pfizer Canada Inc.*, 2010 FCA 242 (*Pfizer*), where Nadon J.A., writing for the Court concluded (at para. 100) that the judge

> … may have misapplied the "mere scintilla" test because in the present matter, there had been a specific promise that sildenafil would work to treat [erectile dysfunction].

However, he said, since the judge had found that there was more than a scintilla of utility, "his error does not attract our intervention."

[34] The question is whether Lilly had sufficient evidence in 1996 to establish that atomoxetine would deliver on the promise of the patent. The Judge concluded that Teva had established that the answer to this question was, no. I see no reversible error in his determination of this essentially factual question.

[35] The Judge specifically stated (at para. 93) that the proof required to demonstrate utility for the purpose of obtaining a patent is less than that required to satisfy the Minister of Health of the efficacy of a medicine for a specified use in order to obtain permission to market it. Rather, on the basis of the testimony of the expert witness whom he found most credible, the Judge concluded that the clinical trial had serious methodological limitations, particularly its short duration and small sample, shortcomings that were also acknowledged by the authors of the MGH Study.

[36] The Judge agreed that the data from this pilot study were promising, and "indicated a clinically and statistically significantly response rate for atomoxetine over placebo" (at para. 20). Nonetheless, the patent promised that atomoxetine was an effective treatment of ADHD, that is, it would alleviate manifestations of the disorder in some patients to such a degree that a doctor would consider prescribing it. The Judge was not prepared to infer from the limited experimental data and

the nuanced conclusions of the authors of the reports of the MGH Study that there was sufficient evidence that atomoxetine was a clinically effective treatment of ADHD.

[37] The fundamental question in dispute at the trial was whether the MGH Study - the only study conducted prior to the issue of the patent - demonstrated that, as promised in the patent, atomoxetine was a clinically effective treatment of ADHD. The Judge clearly set out the opposing views (at para. 9) as follows:

> Dr. Virani described the MGH Study as a pilot with so many methodological limitations that its data were only preliminary and, at best, interesting. According to Dr. Virani, a far more exacting clinical trial would have been needed to establish atomoxetine's effectiveness as an ADHD drug. Dr. McGough's contrary view was essentially that the MGH Study data were proof of atomoxetine's efficacy because they showed, in a statistically significant way, that atomoxetine had worked to treat several of the patients studied for at least the duration of the trial.

[38] Having examined the evidence, the Judge concluded (at para. 113):

> For the most part, I accept Dr. Virani's evidence about the limitations of the MGH Study and find that its reported results do not demonstrate the clinical utility of atomoxetine to treat ADHD in adults let alone in children and adolescents. This was a clinical trial that was too small in size and too short in duration to provide anything more than interesting but inconclusive data. With a patient sample of this uniformity and size, an exposure to atomoxetine of only three weeks and a degree of subjectivity in the testing, one can only conclude, as the researchers themselves stated, that the study had "limitations" and the results were promising but only preliminary.

[39] It is also relevant that, on the basis of the MGH Study, Lilly did not immediately proceed with the development of atomoxetine. Rather, atomoxetine was one of three compounds which Lilly considered as possible treatments of ADHD, before finally selecting atomoxetine. Lilly's

contemporaneous conduct does not suggest that it viewed the MGH Study as demonstrating that atomoxetine was an effective treatment of ADHD.

[40] In reaching his conclusion that utility had not been demonstrated, the Judge also took into account Lilly's previous experience with atomoxetine for treating depression. Early clinical trials with human subjects had indicated very positive results for this use, as had subsequent studies that were more elaborate than the MGH Study in the present case. Nonetheless, Lilly abandoned this project in 1991 when researchers were unable to replicate these results. After that, Lilly considered the possibility that atomoxetine might be useful in the treatment of ADHD.

[41] Counsel for Lilly relied on the decision of this Court in *Pfizer*, which was released shortly after the decision of the Judge in the present case. He argued that this Court had upheld the trial judge's finding that a clinical study had demonstrated that the medicine in question, VIAGRA, was an effective treatment for erectile dysfunction. He noted that the study in that case was also described as a pilot study and involved only sixteen patients, and that its results did not reach statistical significance.

[42] However, utility is largely a question of fact that is decided in each case on the basis of the evidence and the judge's assessment of it. That a judge in one case concluded that utility was shown on the basis of the evidence before her is of little value in persuading an appellate court that a judge in another case, where the evidence was somewhat similar, must have applied too high a standard of proof or committed a palpable and overriding error because he reached the opposite result.

[43] In my opinion, the Judge made no palpable and overriding error in concluding that the evidence was insufficient, for patentability purposes, to demonstrate the effectiveness of atomoxetine as a clinical treatment for ADHD.

(iv) *Burden of proof*

[44] The parties agree that the party challenging the validity of a patent has the burden of proving that it is invalid, and the Judge so held (at paras. 28 and 31). Thus, Teva had the burden of proving that, when the ’735 patent was filed, the evidence was insufficient to demonstrate that atomoxetine would treat ADHD.

[45] Lilly submitted in its memorandum of fact and law that, although the Judge correctly stated the law, in fact he reversed the burden by requiring Lilly to prove the utility of the patent. I see nothing in the Judge’s reasons to support this allegation. Indeed, in oral argument counsel seemed not to press this point.

(v) *Prediction of utility and the need for disclosure*

[46] After concluding that Teva had established that atomoxetine was not useful because it had not been demonstrated to be an effective treatment for ADHD, the Judge considered whether a POSITA would be able soundly to predict the claimed utility. He held that Lilly could not rely on the principle of sound prediction because it had not disclosed *in the patent* the MGH Study which was the factual basis of the prediction.

[47] Lilly submits that neither the *Patent Act* nor the Supreme Court's jurisprudence requires disclosure of this kind in the patent as a condition precedent to successfully invoking sound prediction as the basis of the utility of the claimed invention. However, while Justice Binnie may not have definitively decided this question in *Apotex Inc. v. Wellcome Foundation Ltd*., 2002 SCC 77, [2002] 4 S.C.R. 153 at para. 70, it has been held in the Federal Court, and affirmed by this Court, that a patentee must disclose in the patent a study that provides the factual basis of the sound prediction: *Eli Lilly Canada Inc. v. Apotex Inc*., 2008 FC 142, 63 C.P.R. (4th) 406, *aff'd.* 2009 FCA 97, 78 C.P.R. (4th) 388 (*Eli Lilly Canada*).

[48] Counsel argued that Lilly had made an international application for the '735 patent. He relied on Article 27(4) of the *Patent Cooperation Treaty*, 1970, 28 U.F.T 7647 (Treaty), which provides that in matters of form or contents required for national patent applications, an applicant can insist that the relevant provision of the Treaty and Regulations be applied to the international application.

[49] In my view, this argument does not assist Lilly. Article 27(5) of the Treaty provides that nothing in the Treaty or the Regulations shall be construed as limiting Contracting States' freedom to prescribe substantive conditions of patentability. Writing for this Court in *Eli Lilly Canada*, Justice Noël stated (at para. 19):

> The appellant further argues that requiring the complete disclosure of the factual basis underlying the sound prediction is inconsistent with the *Patent Cooperation Treaty*… However, this *Treaty* specifically contemplates the supremacy of national law in setting the rules for substantive conditions of patentability (see article 27(5) of the Treaty). We are concerned here with substantive conditions of patentability.
>
> [Emphasis added]

[50] I see no basis in the present case for departing from the normal practice of this Court to follow its own decisions. The decision in *Eli Lilly Canada* was far from being "manifestly wrong" in any of the senses contemplated by *Miller v. Canada (Attorney General)*, 2002 FCA 370, 220 D.L.R. (4th) 149 at para. 10. In view of his ruling on the applicability of Article 27(5), it is immaterial that Justice Noël did not refer in his reasons to Article 27(4).

[51] Indeed, if disclosure in the patent of the factual basis of the prediction of utility was not required for sound prediction, it would be difficult to see what Lilly could be said to have given to the public, in exchange for the grant of the monopoly, that it did not already have. When utility is based on sound prediction, disclosure of its factual foundation goes to the essence of the bargain with the public underlying patentability.

(v) *Costs*

[52] In supplementary reasons for judgment (2010 FC 1154), the Judge awarded elevated costs to Teva at the upper end of Column IV of Tariff B. While deploring the unusual level of acrimony in this litigation, and the delays caused by tactical manoeuvrings, the Judge concluded that both parties were to blame, and therefore did not take their conduct into account in the award of costs. He did, however, provide guidance on the assessment of costs and disbursements.

[53] Lilly argues that if its appeal is dismissed on the substantive issues, the Judge's award of costs should be set aside. The Judge erred, it submits, in failing to reduce the costs and allowable

disbursements to reflect the fact that Teva increased the expense of the litigation by pleading multiple grounds of invalidity, all but one of which the Judge rejected.

[54] I do not agree. The Judge considered this argument and rejected it (at para. 7), on the ground that success in the action was not divided, and the successful party is not normally penalized for raising issues on which it does not prevail. The Judge also noted that, because of the frequent complexity and unusual expense of patent litigation, costs are regularly awarded on a basis higher than the mid-point of Column III.

[55] I see no error of principle in the Judge's exercise of the broad discretion over the award of costs conferred by rule 400 of the *Federal Courts Rules*, SOR/98-106. Since Teva obtained the relief that it was seeking (a declaration that the '735 patent was void), the Judge was correct to conclude that success was not divided. Nor am I persuaded that the Judge committed a reversible error when he decided not to penalize Teva for unsuccessfully raising multiple grounds of invalidity. In patent litigation, grounds of invalidity are often interrelated.

Conclusions

[56] For these reasons, I would dismiss the appeal with costs.

"John M. Evans"
J.A.

"I agree
Marc Noël J.A."

"I agree
Eleanor R. Dawson J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-387-10
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