Federal Court of Appeal | Cour d'appel fédérale

Date: 20231109

Docket: A-128-22

Citation: 2023 FCA 221

CORAM: **LOCKE J.A.**
MACTAVISH J.A.
MONAGHAN J.A.

BETWEEN:

SANDOZ CANADA INC.

Appellant

and

JANSSEN INC. and ACTELION PHARMACEUTICALS LTD.

Respondents

Heard at Toronto, Ontario, on October 4, 2023.

Judgment delivered at Ottawa, Ontario, on November 9, 2023.

REASONS FOR JUDGMENT BY: LOCKE J.A.

CONCURRED IN BY: MACTAVISH J.A.
MONAGHAN J.A.

Federal Court of Appeal | Cour d'appel fédérale

Date: 20231109

Docket: A-128-22

Citation: 2023 FCA 221

CORAM: **LOCKE J.A.**
MACTAVISH J.A.
MONAGHAN J.A.

BETWEEN:

SANDOZ CANADA INC.

Appellant

and

JANSSEN INC. and ACTELION PHARMACEUTICALS LTD.

Respondents

REASONS FOR JUDGMENT

LOCKE J.A.

I. Overview

[1] This appeal concerns a decision of the Federal Court (2022 FC 715, *per* Justice Christine M. Pallotta) that dismissed allegations by the appellant, Sandoz Canada Inc., that Canadian Patent No. 2,659,770 (the Patent) is invalid on various grounds. The invalidity grounds that Sandoz' memorandum of fact and law raised were that the Patent (i) lacked utility in that utility

had not been demonstrated at the time the application therefor was filed, and the requirements for soundly predicting utility were not met, and (ii) claimed more broadly than the invention disclosed or the invention made. Sandoz also argued in the alternative that, if the Patent is not invalid for lack of utility or overbreadth, then it must be invalid for obviousness.

[2] In oral submissions, Sandoz addressed only the lack of utility argument and urged the Court to focus on that argument.

[3] For the reasons discussed below, I would dismiss the present appeal.

II. The Patent and the Federal Court's Decision

[4] The Patent concerns the treatment of vasoconstrictive diseases, including one called pulmonary arterial hypertension (PAH), by a combination of macitentan, which is an endothelin receptor antagonist (ERA), and a phosphodiesterase type-5 inhibitor (PDE5 inhibitor).

[5] The Federal Court addressed allegations of obviousness, lack of utility, overbreadth, and insufficiency.

[6] On all of these issues, the Federal Court identified the correct legal test and concluded that invalidity had not been proven.

[7] On lack of utility, the Federal Court acknowledged the requirement that, at the time of filing the application for a patent, utility must have been demonstrated or the requirements for a

sound prediction of utility must be met. It found that, though utility had not been demonstrated, the requirements for soundly predicting utility were met, and hence the lack of utility argument failed. The relevant requirements for sound prediction were identified in *Apotex Inc. v. Wellcome Foundation Limited*, 2002 SCC 77, [2002] 4 S.C.R. 153 at para. 70 (*Wellcome*), and correctly cited as follows by the Federal Court, which stated that there must be:

> A. A factual basis for the prediction;
>
> B. An articulable and sound line of reasoning from which the desired result can be inferred from the factual basis; and
>
> C. Proper disclosure.

[8] Of particular importance to Sandoz' appeal, the Federal Court did not mention the decision of this Court in *Eli Lilly Canada Inc. v. Novopharm Limited*, 2010 FCA 197, 405 N.R. 1 (*Eli Lilly*), and the following passage therein:

> [84] [*Wellcome*] does not define the threshold required for sound prediction. However, Binnie J. states that more than mere speculation is required (para. 69). He also provides the following indicia:
>
> - the requirement is that the claims be fairly based on the patent disclosure (para. 59);
> - it must be *prima facie* reasonable that the patentee should have a claim (para. 60);
> - it cannot mean a certainty (para. 62);
> - the desired result must be able to be inferred from the factual basis (para. 70).
>
> [85] In my view, these indicia signify that a sound prediction requires a *prima facie* reasonable inference of utility…

[9] Sandoz argues that, not only did the Federal Court fail to mention *Eli Lilly*, but it appears to have failed to recognize the requirement therein that, for a prediction to be sound, a party must establish "a *prima facie* reasonable inference of utility." Sandoz argues that the Federal Court erred by applying a lower threshold for sound prediction.

III. Standard of Review

[10] The parties agree, and I concur, that the standard of review to be applied by this Court is the normal appellate standard as set out in *Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R. 235 (*Housen*). Questions of law are reviewed on a standard of correctness, and questions of fact or of mixed fact and law, from which no legal question is extricable, are reviewed on a standard of palpable and overriding error. A palpable error is one that is obvious. An overriding error is one that goes to the very core of the outcome of the case. It is not enough to pull at leaves and branches and leave the tree standing. The entire tree must fall: *Benhaim v. St-Germain*, 2016 SCC 48, [2016] 2 S.C.R. 352 at para. 38, quoting from *Canada v. South Yukon Forest Corporation*, 2012 FCA 165, 431 N.R. 286 at para. 46. A palpable and overriding error is in the nature not of a needle in a haystack, but a beam in the eye: *Benhaim* at paragraph 39, quoting from *J.G. v. Nadeau*, 2016 QCCA 167, [2016] J.Q. No. 635 (QL) at para. 77.

[11] At the hearing of this appeal, Sandoz characterized the sole issue raised by the appeal as being a legal question, extricable from the question of mixed fact and law of whether there was a sound prediction of utility. The extricable legal question is whether the Federal Court applied the incorrect legal test for sound prediction by failing to consider the requirement for a *prima facie*

reasonable inference of utility. Sandoz submits that the appropriate standard of review to be applied to this question is correctness. Sandoz does not argue that the Federal Court made a palpable and overriding error.

[12] Sandoz argues that its position is similar to the example cited in *Housen* at paragraph 27 and quoted from *Canada (Director of Investigation and Research) v. Southam Inc.*, [1997] 1 S.C.R. 748, 144 D.L.R. (4th) 1 at para. 39:

> [I]f a decision-maker says that the correct test requires him or her to consider A, B, C, and D, but in fact the decision-maker considers only A, B, and C, then the outcome is as if he or she had applied a law that required consideration of only A, B, and C. If the correct test requires him or her to consider D as well, then the decision-maker has in effect applied the wrong law, and so has made an error of law.

IV. Analysis

A. *Principal Argument: Threshold for Sound Prediction*

[13] Sandoz' focus on extricable questions of law keeps the bar low for finding a reviewable error, but it prevents it from challenging factual findings by the Federal Court. We cannot review factual findings on a correctness standard. This is important because the Federal Court did not explicitly misstate the applicable legal test. Rather, Sandoz asks this Court to infer that the Federal Court applied the wrong test. It notes the Federal Court's failure to mention the "*prima facie* reasonable inference of utility" requirement. It relies also on the evidence that was adduced at trial.

[14] At this point, it is advisable to look again at the statement in *Eli Lilly* (on which Sandoz relies), and at *Wellcome*, which inspired the statement. Clearly, *Eli Lilly* was not purporting to change the legal test set out in *Wellcome*. Rather, it was attempting to glean, from the reasons in *Wellcome*, the appropriate threshold for finding that a prediction is sound. This Court in *Eli Lilly* expressed the "*prima facie* reasonable inference of utility" requirement based on cited passages from paragraphs 59, 60, 62, 69 and 70 of *Wellcome*.

[15] Sandoz also cites several additional passages from *Wellcome* that indicate what is not sufficient for a prediction to be sound:

1. No more than a mere belief that something might be useful (para. 25);

2. Little more than an announcement of a research project (para. 64); and

3. Only a promise that a hypothesis might later prove useful (para. 84).

[16] In my view, there is nothing in *Eli Lilly* that represents any kind of departure from what one would glean from a complete reading of *Wellcome*. While it is not necessary that the prediction be certain (see *Wellcome* at paragraph 62), or to a regulatory standard (see *Wellcome* at paragraph 63), the public is entitled to a teaching that is solid (see *Wellcome* at paragraph 69) and accurate and meaningful (see *Wellcome* at paragraph 83), and based not on speculation but exact science (see *Wellcome* at paragraph 84).

[17] Turning now to the reasons for the Federal Court's decision under appeal, I note that paragraphs 207 to 209 thereof refer explicitly and repeatedly to *Wellcome*, and specifically to paragraphs 56, 62, 66, 70 and 77 thereof. Clearly, the Federal Court read and considered *Wellcome* as a whole, and not just the three requirements for sound prediction as enumerated at paragraph 7 above. It would be difficult to conclude that, despite having carefully reviewed so much of *Wellcome*, the Federal Court overlooked the paragraphs that led to the "*prima facie* reasonable inference of utility" requirement.

[18] Sandoz acknowledges that the Federal Court did not err simply in failing to state that the threshold for a sound prediction is a *prima facie* reasonable inference of utility. However, Sandoz urges this Court to infer that the Federal Court failed to apply this threshold because, it says, the evidence could not support it.

[19] Sandoz cites 11 factual findings made by the Federal Court (with which it does not take issue) in support of its position:

A. Pulmonary hypertension is a general term that describes abnormally high blood pressure in the pulmonary circulatory system (see paragraph 118 of the Federal Court's reasons);

B. PAH is a subtype of pulmonary hypertension where the constricted walls of the arteries of the lungs increase vascular resistance to blood flow. If left untreated, the increased pressure strains the right side of the heart, which is responsible for pumping

blood to the lungs, leading to heart failure (see paragraph 118 of the Federal Court's reasons);

C. One PDE5 inhibitor (sildenafil) was approved to treat PAH, and another (tadalafil) had been approved to treat erectile dysfunction and was sometimes prescribed off label for PAH (see paragraph 128 of the Federal Court's reasons);

D. Two ERAs (bosentan and sitaxsentan) were approved to treat PAH (see paragraph 128 of the Federal Court's reasons);

E. No clinical trial had been conducted or published on the combination of an ERA and a PDE5 inhibitor. Treatment guidelines from professional organizations did not recommend any combination treatments for PAH (see paragraph 146 of the Federal Court's reasons);

F. The medical field had not reached a consensus about combination therapy and its role in treatment, and was watching the developments, but acknowledged that important questions had not been answered (see paragraph 157 of the Federal Court's reasons);

G. These were early days for PAH therapies and the evidence in support of combination treatment was limited (see paragraph 165 of the Federal Court's reasons);

H. The published results of a long-term study in nine human patients suffering from PAH who were treated with a combination of bosentan (an ERA) and sildenafil (a PDE5 inhibitor) provided nothing more than preliminary (rather than definitive)

evidence that this specific combination worked for patients who participated in the study (see paragraph 153 of the Federal Court's reasons);

I. The skilled person would not have expected the combination of any ERA with a PDE5 inhibitor to be useful for treating diseases involving vasoconstriction, including PAH. As questions remained on the key point of whether the results were due to the combination of bosentan and sildenafil, the skilled person would consider that there was not an acceptable level of confidence that these drugs were effective as a combination therapy (see paragraphs 159 and 165 of the Federal Court's reasons);

J. The skilled person would have considered the evidence insufficient to extrapolate the teachings about bosentan and sildenafil to a combination of any ERA and a PDE5 inhibitor, based on shared mechanisms of action (see paragraph 159 of the Federal Court's reasons); and

K. Macitentan was effectively unknown to the skilled person (see paragraph 193 of the Federal Court's reasons).

[20] Sandoz emphasizes that the Federal Court found that long-term studies in humans with PAH were insufficient to provide more than preliminary evidence (rather that definitive evidence) that combination treatment would be effective. As the Federal Court based its conclusion of sound prediction on studies on rats (not humans), which were based on systemic (rather than pulmonary) blood pressure results, Sandoz argues that the Federal Court could not have had the threshold requirement of *prima facie* reasonable inference of utility in mind. As stated by Sandoz, the rat studies provided only a promise that a hypothesis might later prove

useful, which *Wellcome* at paragraph 84 indicated is insufficient to support a finding of utility based on a sound prediction.

[21] Sandoz also argues that the factual evidence before the Federal Court likewise provided insufficient support for finding a *prima facie* reasonable inference of utility. It notes that the respondents' own expert witnesses never referred to this requirement, and were not instructed to consider it when forming their opinions. Sandoz argues that, in support of their opinions, these experts went no further than saying that the rat studies described in the Patent provided a positive signal to the skilled person that macitentan in combination with a PDE5 inhibitor may be used for treating a disease where vasoconstriction is involved.

[22] Sandoz argues that the Federal Court's reliance on this "positive signal" opinion indicates that its conclusion with respect to the issue of sound prediction was based on the wrong legal test.

[23] The question for the Court in this appeal is whether the circumstances suggest that the Federal Court applied a lower threshold for sound prediction than that contemplated in *Wellcome* and *Eli Lilly*. In my view, the answer is no.

[24] The threshold is not high. The terms "*prima facie*" and "reasonable inference" leave considerable space for a fact-finding body in reaching its conclusion. In view of the fact that the Federal Court was clearly familiar with the teachings in *Wellcome*, I am not prepared to conclude that it overlooked the guidance therein that the teaching in a patent based on a sound prediction

must be solid, accurate and meaningful, and based on exact science (not speculation): *Wellcome* at paragraphs 69, 83 and 84. The Federal Court's reasons indicate that it was satisfied in this regard.

[25] I do not accept Sandoz' argument that, at the time of filing the application for the Patent, the inventors necessarily had no more than a promise that a hypothesis might later prove useful. The fact that more experimentation was required after the rat studies did not necessarily take the utility of the invention outside the scope of a sound prediction. The doctrine of sound prediction, in its nature, presupposes that further work remains to be done: *Wellcome* at paragraph 77. It was up to the Federal Court to weigh the evidence and decide whether the threshold for a sound prediction was met.

[26] I also do not accept Sandoz' suggestion that the Federal Court's finding that published long-term human studies were no more than preliminary evidence that the combination of bosentan and sildenafil would be effective in treating PAH is inconsistent with the conclusion that one could draw a *prima facie* reasonable inference of utility from rat studies measuring systemic (not pulmonary) blood pressure.

[27] First, the Federal Court's use of the term "preliminary evidence" was made in the context of its analysis of obviousness, not sound prediction, and was used to contrast "definitive evidence." Read in context, the Federal Court's conclusion was that the human studies did not provide definitive evidence that the combination of bosentan and sildenafil would be effective. Moreover, the legal tests for obviousness and for sound prediction are distinct and different;

common general knowledge may be sufficient to support a sound prediction, but not sufficient to find obviousness: *Pharmascience Inc. v. Teva Canada Innovation*, 2022 FCA 2, [2022] F.C.J. No. 3 (QL) at para. 38.

[28] Second, the Patent concerns a combination of a different ERA (macitentan) with a PDE5 inhibitor than was tested in the human studies. In the context of the Federal Court's analysis of obviousness, this is notable.

[29] Third, I am not prepared, any more than the Federal Court was, to conclude that the fact that the rat studies measured systemic blood pressure rather than pulmonary blood pressure is a difference sufficient to prevent a sound prediction of utility on the record before the Federal Court. I conclude similarly with regard to the fact that the Patent concerns treatment of humans, whereas the rat studies concerned rats. Sandoz acknowledges that animal studies can be the basis of a sound prediction of utility in humans.

[30] In conclusion, the factual conclusions cited by Sandoz, and enumerated in paragraph 19 above, do not lead me to conclude that the Federal Court applied a threshold for sound prediction lower than a *prima facie* reasonable inference of utility. The Federal Court's failure to cite this wording is not remarkable, and does not amount to an error of law. The respondents cite examples of decisions, including from this Court, that deal with the issue of sound prediction without mentioning this wording: *Teva Canada Limited v. Leo Pharma Inc.*, 2017 FCA 50; *Packers Plus Energy Services Inc. v. Essential Energy Services Ltd.*, 2017 FC 1111, [2017]

F.C.J. No. 1200 (QL), aff'd 2019 FCA 96, [2019] F.C.J. No. 459; *Apotex Inc. v. Allergan Inc.*, 2015 FCA 137, [2015] F.C.J. No. 953 (QL).

[31] I note that Sandoz itself did not explicitly refer to this wording in its written argument before the Federal Court, referring to it only obliquely by reference to the relevant paragraphs from *Eli Lilly*. In this context, it is not surprising that the Federal Court was not led to use this wording.

B. *Other Arguments*

[32] Though Sandoz has asked this Court to focus on its principal argument as the basis for its appeal, I note that I have considered all of the arguments that were raised in Sandoz' memorandum of fact and law, and have found none has merit.

V. Conclusion

[33] It follows from the foregoing that the appeal should be dismissed. I would do so with costs to the respondents in the agreed upon amount of $15,000.

[34] In closing, I take this opportunity to thank the parties for their very able submissions and for their work to trim the issues in dispute. This has not only assisted the Court in releasing a

decision in this appeal with a minimum of delay, but I believe it has benefited the parties by focussing on the issues most likely to affect the outcome.

"George R. Locke"
J.A.

"I agree
Anne L. Mactavish J.A."

"I agree
K.A. Siobhan Monaghan J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKET:	A-128-22
STYLE OF CAUSE:	SANDOZ CANADA INC. v. JANSSEN INC. and ACTELION PHARMACEUTICALS LTD.
PLACE OF HEARING:	TORONTO, ONTARIO
DATE OF HEARING:	OCTOBER 4, 2023
REASONS FOR JUDGMENT BY:	LOCKE J.A.
CONCURRED IN BY:	MACTAVISH J.A. MONAGHAN J.A.
DATED:	NOVEMBER 9, 2023

APPEARANCES:

Andrew Brodkin Jordan Scopa	FOR THE APPELLANT
Andrew Skodyn Melanie Baird Dylan Churchill	FOR THE RESPONDENTS

SOLICITORS OF RECORD:

Goodmans LLP Toronto, Ontario	FOR THE APPELLANT
Blake, Cassels & Graydon LLP Toronto, Ontario	FOR THE RESPONDENTS