Federal Court of Appeal  Cour d'appel fédérale

Date: 20210304

Docket: A-437-19

Citation: 2021 FCA 45

CORAM: **WEBB J.A.**
BOIVIN J.A.
LOCKE J.A.

BETWEEN:

APOTEX INC.

Appellant

and

JANSSEN INC., JANSSEN ONCOLOGY INC., BTG INTERNATIONAL LTD. and THE MINISTER OF HEALTH

Respondents

Heard by online video conference hosted by the registry on January 20, 2021.

Judgment delivered at Ottawa, Ontario, on March 4, 2021.

REASONS FOR JUDGMENT BY: LOCKE J.A.

CONCURRED IN BY: WEBB J.A.
BOIVIN J.A.

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REASONS FOR JUDGMENT

LOCKE J.A.

I. Background

[1] This is an appeal of a decision of the Federal Court (2019 FC 1355, per Phelan J.), which granted an application by the respondents Janssen Inc., Janssen Oncology Inc. and BTG

International Ltd. (collectively, Janssen) pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, S.O.R./93-133 (the Regulations), as they stood prior to September 21, 2017. The Federal Court's judgment prohibited the Minister of Health from granting marketing authorization (a notice of compliance, or NOC) to the appellant, Apotex Inc. (Apotex), for its APO-ABIRATERONE product.

[2] APO-ABIRATERONE is Apotex's version of a drug product marketed by Janssen under the name ZYTIGA. Canadian Patent No. 2,661,422 (the 422 Patent) was listed on the Patent Register (established under the Regulations) for ZYTIGA. Under the Regulations, Apotex was required to address the 422 Patent before obtaining an NOC for APO-ABIRATERONE. Apotex alleged that the 422 Patent is invalid (for lack of patentable subject matter, for obviousness, and for inutility), would not be infringed, and is ineligible to be listed on the Patent Register. The Federal Court found in favour of Janssen on all of these issues. Apotex now appeals the Federal Court's decision.

[3] It is interesting to note that, following amendments to the Regulations that came into force on September 21, 2017, a second Federal Court proceeding under the Regulations concerning the 422 Patent was commenced. Pursuant to those amendments, the second proceeding was in the form of an action, with a trial and live witnesses. By contrast, the first proceeding (which led to the decision under appeal) was an application, in which witnesses gave evidence by affidavit and were cross-examined outside of court. The second proceeding involved Apotex as well as other parties seeking to market their versions of ZYTIGA. The trial in the second proceeding was presided over by the same judge as in the first (Phelan J.) and led to a

decision dated January 14, 2021 (2021 FC 7). This second decision found, contrary to the first, that the 422 Patent is, and always has been, invalid for obviousness. Though some of the witnesses were the same, and some of the documents they referred to were the same, the evidentiary record in each of the proceedings is distinct, and the present appeal must be decided based on the record in the first proceeding.

[4] Another notable fact related to the second proceeding is that, following the declaration of invalidity of the 422 Patent, the Minister of Health issued an NOC for APO-ABIRATERONE. Since the decision under appeal merely prohibited the Minister of Health from doing so, the present appeal is now moot. However, the parties agree that this appeal should be decided despite its mootness. Apotex notes that this Court's decision could be relevant to its right, under section 8 of the Regulations, to make a claim against Janssen for losses Apotex suffered because of the delay in obtaining its NOC. Apotex cites this Court's decision in *Apotex Inc. v. Bayer AG*, 2004 FCA 242, 78 C.P.R. (4th) 428 as a precedent for hearing a moot appeal in these circumstances. I agree with the parties that this Court should exercise its discretion to decide the present appeal despite its mootness.

[5] For the reasons provided below, I have concluded that the present appeal should be dismissed.

II. Patented Technology

[6] I preface this section by noting that the 422 Patent concerns very complex technology, and this section provides only minimum limited amount of information necessary to understand

the issues in dispute. This section is drawn principally from the Federal Court's description of the 422 Patent and the scientific background and common general knowledge related thereto. It is clear from the Federal Court's reasons (the Reasons) that it had a good understanding of this subject. Neither party disputes that.

[7] The 422 Patent, as well as the ZYTIGA and APO-ABIRATERONE products, concern a treatment for prostate cancer. At the dates relevant to the validity of the 422 Patent (August 25, 2006 for obviousness, August 23, 2007 for inutility, and February 28, 2008 for claim construction), the primary treatment for prostate cancer was androgen deprivation therapy (ADT) to suppress the production of male sex hormones (androgens), specifically testosterone, in the testes. Testosterone was known to promote the growth of cancer cells. However, testosterone is also produced in the adrenal gland. Because of this, patients treated with ADT eventually see a resumption in the progress of their cancer. Such a cancer is commonly referred to as castration resistant prostate cancer (CRPC) (Reasons, para. 17).

[8] What causes prostate cancer to become castration resistant was not fully understood in 2007. Secondary hormonal therapy by suppressing residual androgen production in the adrenal gland was an active area of research (Reasons, para. 99). However, the adrenal gland also produces other hormones, such as glucocorticoids. Androgen production in the adrenal gland could be reduced, but this could cause certain potentially serious side effects of suppressed glucocorticoid production. It was known that adrenal androgen inhibitors ketoconazole (KC) and aminoglutethimide (AG) could have some short-term anti-cancer effects for late-stage prostate cancer patients, although with serious side effects (Reasons, para. 102).

[9] It was also known to co-administer a glucocorticoid to minimize these side effects. The most commonly administered such glucocorticoids were prednisone (PN) and dexamethasone. Administration of such drugs is called glucocorticoid replacement therapy. PN was also sometimes used at the time for its palliative effects, but only as a last resort because of concerns that it would limit the ability of the adrenal gland to produce glucocorticoids (Reasons, para. 77). PN was not generally known on its own as an effective treatment for prostate cancer (Reasons, para, 111), but it was commonly known to have modest anti-cancer effects (Reasons, para. 135).

[10] It was commonly known that an adrenal androgen inhibitor that was more selective than KC or AG in inhibiting androgen production (rather than glucocorticoid production) could more effectively treat prostate cancer with fewer expected side effects (Reasons, para. 115). One such more selective adrenal androgen inhibitor was abiraterone acetate (AA). The 17α-hydroxylase/ $C_{17,20}$-lyase (CYP17) enzyme has two activities in adrenal steroid (hormone) synthesis: 17α-hydroxylase activity and 17,20-lyase activity. 17α-hydroxylase activity is necessary for the production of cortisol (the body's major glucocorticoid) as well as androgens. 17,20-lyase activity only affects the production of androgens (Reasons, para. 26). AA is a CYP17 enzyme inhibitor that preferentially inhibits the 17,20-lyase activity of CYP17 and thus allows for the production of cortisol to continue. Therefore, there was no reason in 2007 to think that glucocorticoid replacement therapy would be needed with AA treatment (Reasons, para. 80).

[11] The 422 Patent concerns the treatment of prostate cancer by administering AA in combination with PN. As construed by the Federal Court, the claims require that both the AA and PN components be in a "therapeutically effective amount". As defined in the 422 Patent, this

means an amount effective for “treating” prostate cancer, where “treat” covers a broad range of results from eradication of a tumour to delay of the spread of cancer. The Federal Court interpreted “therapeutically effective amount” as sufficient to attack the cancer in a meaningful way: Reasons, para. 123. Practically speaking, this requires that the PN not act simply as a palliative drug.

[12] In 2005, the owner of the 422 Patent, then known as Cougar Biotechnology Inc., began to study the use of AA for treatment of CRPC. The working hypothesis was that adding a glucocorticoid could reduce production of upstream precursor adrenal steroids, reverse resistance to AA, and therefore have anti-cancer activity (Reasons, para. 40). In a first study (called COU-AA-001 or the 001 Study), a single patient responded positively to treatment with a combination of AA and the glucocorticoid dexamethasone. Though AA was effective in treating prostate cancer alone (Reasons, para. 215), the combination was better. This result was characterized by the lead researcher as “surprising and unexpected”, and it supported the working hypothesis. A further study, called COU-AA-004 or the 004 Study, evaluated the combination of AA and the particular glucocorticoid of relevance to the 422 Patent, PN. The results of the 004 Study confirmed the effectiveness of this combination in treating CRPC.

III. Issues

[13] The issues in dispute in this appeal can be divided into four categories:

A. Patentable Subject Matter
B. Obviousness
C. Inutility
D. Infringement

IV. Analysis

[14] Before entering into an analysis of the issues in dispute, it may be helpful to note some issues that are not disputed.

[15] The parties do not disagree on the standard of review. They agree that questions of law are reviewed on a standard of correctness, and questions of fact or of mixed fact and law (absent an extricable question of law) are reviewed on a standard of palpable and overriding error: see *Housen v. Nikolaisen*, 2002 SCC 33, [2002] 2 S.C.R. 235 at paras. 8, 10, 26 (*Housen*).

[16] Apotex does not take issue with the Federal Court's analysis of the burden of proof and the legal tests applicable to the issues of obviousness, inutility and infringement.

[17] Apotex also does not dispute the Federal Court's findings concerning the skills of the person of ordinary skill in the art (the POS), the common general knowledge, and the construction of the claims in issue.

A. *Patentable Subject Matter*

[18] The Federal Court concluded that the 422 Patent claims patentable subject matter because the claimed combination of AA and PN achieves an anti-cancer effect that is greater than with either drug alone.

[19] Apotex takes issue with the Federal Court's comparison of the results obtained with the combination to the results obtained with either drug alone. Apotex argues that the comparison of the combination should instead be with the sum of the two component drugs (Apotex calls this synergy). In support of this contention, Apotex cites *R. v. American Optical Co.*, [1950] Ex C.R. 344, 13 C.P.R. 87 at 98-99 (*American Optical*); *Eli Lilly Canada Inc. v. Apotex Inc.*, 2018 FC 736, 156 C.P.R. (4th) 387 at paras. 71-72 (*Eli Lilly*). Citing *American Optical*, *Eli Lilly* stated, "it is essential to the validity of a patent for a combination that the combination should lead to a unitary result, and that such result should be different from the sum of the results of the elements." Apotex uses the term "synergy" to describe the requirement, but it appears that it sees no difference between this term and the requirements for unitary result and improved results over the sum of the components of a combination.

[20] For its part, Janssen argues that the requirements for a unitary result and improved results with the combination do not properly relate to the question of patentable subject matter, and are more appropriate to consider in the context of analysis of other validity issues such as anticipation or obviousness. Janssen argues that the Exchequer Court and Federal Court authorities cited by Apotex are incorrect in law because they failed to have regard to binding Supreme Court of Canada authorities and the wording of the *Patent Act*, R.S.C. 1985, c. P-4. They assert that any requirement for patentability must be grounded in the *Patent Act*, and nothing in the definition of "invention" in section 2 thereof, or elsewhere, requires a unitary result in the case of a combination invention. Janssen also argues that the decisions in *Baldwin International Radio Co. of Canada, Ltd. v. Western Electric Co., Inc.*, [1934] S.C.R. 94, [1934] 1

D.L.R. 369 at 100-101, and *R. v. Uhlemann Optical Co.*, [1952] 1 S.C.R. 143, 15 C.P.R. 99 dealt with the question of the result of the combination as part of the anticipation analysis.

[21] Janssen points out that a claim for the use of AA alone to treat prostate cancer would be patentable subject matter, although it would likely fail for anticipation and obviousness. The same is true of the use of PN alone. If each of the components of the claimed combination constitutes patentable subject matter, Janssen asks, how could one reasonably conclude that the combination does not.

[22] Janssen's argument is an interesting one. However, this is not the case to decide the issue. In my view, the combination claimed in the 422 Patent meets even the requirements set out in *American Optical* and *Eli Lilly*. It is clear that the Federal Court accepted that the combination of AA and PN achieves results in the treatment of prostate cancer that are not achieved with either drug alone. I disagree with Apotex's argument that finding a unitary result in the combination claimed in the 422 Patent necessarily requires comparison to the sum of the results achieved with the component drugs. In the context of the treatment of cancer, it is feasible to compare to results achieved with each drug alone, but there is no concept of a sum of these results to which the combination could be compared.

[23] Apotex suggests that measurements of success in cancer treatment could simply be added together to determine a sum. Apotex suggests PSA (prostate specific antigen) results, for example. However, such an addition would not yield useful information where, as with PSA results, success is measured by a reduction in the number. The same would be true if one were to

measure tumour growth. It cannot be that a combination can be excluded from patentability simply because it is not susceptible to comparison with the sum of the component parts. The key consideration should be whether the combination offers something that was not available to the public before. An aggregation is problematic because it does not provide more than was already available to the public. Though there is dispute about whether this was demonstrated prior to the filing date of the 422 Patent (this issue is addressed in discussion below on the inutility allegation), there is no dispute that the combination in issue provides improved results over what was previously known.

B. *Obviousness*

[24] Apotex argues that claims to the treatment of CRPC using a combination AA and PN should have been found obvious because AA's mechanism of action, as an adrenal androgen inhibitor was similar to KC and AG, and hence the POS would have been wary of the potential for side effects requiring glucocorticoid replacement therapy, such as with PN. Moreover, the POS would have been aware of the modest anti-cancer effects of PN.

[25] Apotex makes several arguments concerning legal principles applicable to obviousness analysis. First, Apotex argues that obviousness is to be assessed by asking whether the distance between two points (the state of the art and the subject matter of the claim in question) can be bridged by the POS. Apotex argues that the second point (the subject matter of the claim) is to be determined by reference to the language of the claim. This is consistent with section 28.3 of the *Patent Act* and with the jurisprudence. Apotex also argues that the first point (the state of the art) is to be determined by reference not to the prior art at large, but rather to the prior art chosen by

the party alleging obviousness. However, I do not understand the authorities cited by Apotex in support of this argument to limit the scope of prior art that can be considered for obviousness.

[26] Apotex also argues that the ultimate question in the obviousness analysis is not whether the subject matter of the specific claim itself is obvious, but rather whether the difference between it and the state of the art can be bridged by the POS using only their common knowledge and other information they could have found (see paragraph 41 of Apotex's factum). I see no distinction here. Per section 28.3 of the *Patent Act*, the ultimate question is whether the "subject-matter defined by a claim" is "obvious […] to a person skilled in the art or science to which it pertains" having regard to the relevant prior art. Contrary to Apotex's assertion, the focus of the analysis is indeed on whether the subject matter of the specific claim itself is obvious. That said, the obviousness of the claim may be assessed by considering whether the difference between the state of the art and the subject matter of the claim can be bridged by the POS.

[27] Apotex criticizes the Federal Court for looking beyond the scope of the claims in its obviousness analysis. Specifically, Apotex cites the Federal Court's observations that (i) neither AA nor PN had shown a survival benefit; (ii) there was no well-understood mechanism of action for PN's anti-cancer effect; (iii) no prior art suggested that AA would be more effective in treating cancer if combined with another drug; (iv) no prior art hypothesized that glucocorticoids might prevent resistance to treatment with AA (see paragraph 53 of Apotex's factum). These observations were made by the Federal Court in paragraph 178 of the Reasons, as part of a discussion of differences between the state of the art and the invention. Though some of these

observations may not relate to elements of the claims in issue, I see no reviewable error in making the observations. As argued by Janssen, they are relevant to determining what the POS seeking a better treatment for CRPC would have considered. Apotex argues that these observations by the Federal Court might be relevant to whether the POS would have been able to bridge the difference between the state of the art and the invention, but it was improper to make these observations in defining that difference (or as Apotex put it, setting the goalposts). However, the setting of the "goalposts" is not in dispute; the parties do not dispute the state of the art or the subject matter of the claims. Accordingly, paragraph 178 of the Reasons was not defining the difference, and was rather describing some characteristics of it.

[28] Apotex also criticizes the Federal Court for requiring that the POS know the results of certain solutions with certainty. Specifically, Apotex argues that the Federal Court supported its finding at paragraph 185 of the Reasons that the POS would not predict that the combination of AA and PN would have an anti-cancer effect by stating that "[a] POS would not know that the two drugs would not, for example, cancel each other's effectiveness." (emphasis added). I am not prepared to infer from the word "know" in that sentence the requirement of certainty that Apotex urges. I am not convinced that the Federal Court demanded certainty in assessing obviousness.

[29] Further asserting an inappropriate demand for certainty, Apotex notes that the Federal Court refused to find the combination of AA and PN to be obvious, despite acknowledging that the POS would be wary of side effects from the use of AA that might require glucocorticoid replacement therapy, because the prior art had not established the existence of such side effects. A study called O'Donnell 2004 had shown slight effects on cortisol levels (indicative of side

effects of adrenal androgen inhibition), but not enough to take those levels outside the normal range. The Federal Court concluded that the uncertainty about the side effects was such that it would not be obvious to combine AA with a glucocorticoid. In my view, the Federal Court did not err in this conclusion. The POS's wariness about side effects could prompt the Court to consider whether the claimed combination was obvious to try, which it did, but it was not an error to find that the invention was not otherwise obvious.

[30] I turn now to the issue of obviousness to try. Apotex notes, correctly, that an invention is obvious if the POS would have found it obvious to try, and that being more or less self-evident that what is being tried ought to work is merely a factor to be considered and not a requirement. I addressed this same point in *Hospira Healthcare Corporation v. Kennedy Trust for Rheumatology Research*, 2020 FCA 30, 316 A.C.W.S. (3d) 537 at paras. 88-90 (*Hospira*), which issued after the decision under appeal here. I noted that the Supreme Court of Canada in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, [2008] 3 S.C.R. 265 at para. 68 (*Sanofi*) stated that "[i]n areas of endeavour where advances are often won by experimentation, an 'obvious to try' test might be appropriate." I continued by quoting paragraphs 66, 69 and 70 of *Sanofi*:

> [66] For a finding that an invention was "obvious to try", there must be evidence to convince a judge on a balance of probabilities that it was more or less self-evident to try to obtain the invention. Mere possibility that something might turn up is not enough.
>
> […]
>
> [69] If an "obvious to try" test is warranted, the following factors should be taken into consideration at the fourth step of the obviousness inquiry. As with anticipation, this list is not exhaustive. The factors will apply in accordance with the evidence in each case.

> 1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?
>
> 2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?
>
> 3. Is there a motive provided in the prior art to find the solution the patent addresses?
>
> [70] Another important factor may arise from considering the actual course of conduct which culminated in the making of the invention. It is true that obviousness is largely concerned with how a skilled worker would have acted in the light of the prior art. But this is no reason to exclude evidence of the history of the invention, particularly where the knowledge of those involved in finding the invention is no lower than what would be expected of the skilled person.

[31] I concluded as follows at paragraph 90 of *Hospira*:

> It should be noted that, whereas being "more or less self-evident to try to obtain the invention" (per *Sanofi* at para. 66) is a requirement for obviousness to try, being "more or less self-evident that what is being tried ought to work" (per *Sanofi* at para. 69) is not a requirement but merely a factor to be considered.

[32] Apotex argues that the Federal Court made the same error in the present case as it did in *Hospira*. It cites paragraph 195 of the Reasons, which discusses the test for obviousness to try:

> The Court therefore also has to consider whether the combination of AA and PN was more or less self-evident that it ought to work, by examining the extent, nature and amount of effort required to achieve the invention, motive in the prior art to find the solution the patent addresses, and the actual course of conduct of the inventors […]

[33] As phrased, this paragraph does indeed give the impression that the Federal Court considered "more or less self-evident that it ought to work" to be the overarching requirement, with the other factors (extent, nature and amount of effort required, motive to find the solution,

and actual course of conduct) as considerations. However, I am not convinced that the Federal Court made a reviewable error in its obviousness to try analysis.

[34] This case is distinguishable from *Hospira*. There, the Federal Court had treated "more or less self-evident that what is being tried ought to work" as a requirement, and its consideration of at least one of the other factors had been inadequate: *Hospira* at para. 93. In the present case, the Federal Court considered each of the factors relevant to obviousness to try, and reached a conclusion based on that consideration: Reasons, paras. 196-202. While the Federal Court acknowledged that the POS was motivated to develop secondary hormonal therapies to treat CRPC, and to test AA for that purpose, it was not self-evident that the combination of AA and PN would work, and the trials conducted to achieve the invention were not routine. Based on a consideration of the relevant factors, the Federal Court concluded that, though the combination of AA and PN may have been "worth trying", it was not obvious to try. On the standard of palpable and overriding error (which is applicable to this issue of mixed fact and law), this conclusion was open to the Federal Court.

[35] Apotex criticizes the Federal Court's reliance on the 001 Study as an indication of the inventors' actual course of conduct. They note that the glucocorticoid tested was dexamethasone rather than PN. However, the Federal Court was aware of this distinction (Reasons, para. 217). There was no error in viewing this study as a step on the path to the invention.

[36] A final observation on paragraph 195 of the Reasons is that the Federal Court can be forgiven for its lack of clarity as to whether "more or less self-evident that it ought to work"

should be considered a factor in the obviousness to try analysis, or a requirement. The Supreme Court itself gave mixed signals on the point. Before the passages quoted above from *Sanofi*, the Supreme Court stated as follows at paragraph 65: "I am of the opinion that the 'obvious to try' test will work only where it is […] more or less self-evident that what is being tested ought to work." Therefore, it appears that the Supreme Court treated this aspect as a requirement at paragraph 65, and then as a factor at paragraph 69. I maintain my view that "more or less self-evident that it ought to work" should be treated as a factor in the obviousness to try analysis, and not as a requirement. This appears to be more consistent with what the Supreme Court intended.

C. *Inutility*

[37] A valid patent requires utility, though a mere scintilla of utility is sufficient. Utility must be either demonstrated or soundly predicted no later than the filing date of the patent (*Apotex Inc. v. Wellcome Foundation Ltd.*, 2002 SCC 77, [2002] 4 S.C.R. 153 at para. 56; *AstraZeneca Inc. v. Apotex Inc.*, 2017 SCC 36, [2017] 1 S.C.R. 943 at para. 55). In the present case, the Federal Court found that the utility of the invention of the 422 Patent was demonstrated. It also concluded that the requirements for sound prediction of utility were not satisfied.

[38] Apotex challenges the conclusion that utility was demonstrated prior to the filing date of the 422 Patent. There is no challenge to the conclusion concerning sound prediction. Apotex notes that, to establish demonstrated utility, Janssen relied on the 001 and 004 Studies.

[39] While the 004 Study showed that the combination of AA and PN was useful in treating prostate cancer (some patients experienced a drop in PSA levels), it did not compare the results

obtained from the combination with results from the use of either drug alone. Accordingly, the 004 Study is insufficient, on its own, to demonstrate utility of the invention of the 422 Patent.

[40] The 001 Study did include a comparison with the results obtained from the use of AA alone, but the combination tested was AA and dexamethasone (a different glucocorticoid). Accordingly, the 001 Study alone does not demonstrate the utility of the combination claimed in the 422 Patent.

[41] The Federal Court noted the shortcomings of each of the 001 and 004 Studies, but observed that the results thereof have to be interpreted in the context of all of the test results, unless one test conclusively proves that the compound had no utility: Reasons, para. 214; *Teva Canada Ltd. v. Novartis AG*, 2013 FC 141, 428 F.T.R. 1 at paras. 215-216 (*Teva*). I agree with the statement in *Teva* at paragraph 215 that testing should be considered cumulatively when assessing demonstrated utility.

[42] The Federal Court concluded its analysis of demonstrated utility as follows:

> [220] The main issue is whether these studies are enough to show that the combination of drugs was useful, as neither study has a clear comparison that would allow a person to determine that the combination was more effective than either drug taken alone.
>
> [221] However, I have concluded that when considered in the context of the COU-AA-001 study as well as previous studies of the modest anti-cancer effects of PN, they provide evidence of a scintilla of utility of the combination of AA and PN over the anti-cancer effects of AA or PN on their own.

[43] Paragraph 221 indicates that the Federal Court was satisfied that the required scintilla of utility of the invention in issue (being results in treating prostate cancer with the combination of

AA and PN that are better than with either drug alone) was demonstrated by the cumulative effect of the 001 and 004 Studies, as well as "previous studies of the modest anti-cancer effects of PN."

[44] It is useful at this point to note that utility is a question of mixed fact and law, and to recall that the standard of review on such a question is palpable and overriding error. As has been indicated on numerous occasions, "palpable" means "obvious", and "overriding" means "going to the very core of the outcome": *South Yukon Forest Corp. v. R.*, 2012 FCA 165, 4 B.L.R. (5th) 31 at para. 46; *Benhaim v. St-Germain*, 2016 SCC 48, [2016] 2 S.C.R. 352 at para. 38. Therefore, for this Court to intervene on the issue of utility, Apotex must convince us that the Federal Court has made an obvious error that goes to the very core of the outcome.

[45] I recognize that the Federal Court's explanation for its conclusion is short on detail. I understand that the Federal Court was satisfied that the 004 Study showed the utility of the combination of AA and PN as a treatment for CRPC, though without any comparison to show that the combination is better than either drug alone. I also understand that the Federal Court was satisfied that the 001 Study provided a comparison of AA alone with a combination that, though different from the patented combination, is similar (in that both PN and dexamethasone are glucocorticoids). This seems to have satisfied the Federal Court as regards a comparison of the claimed combination to AA alone. The Federal Court also concluded at paragraph 115 of the Reasons that the 001 Study showed that AA was an effective cancer treatment on its own. This is relevant to the requirement, according to the Federal Court's claim construction, that each of the drugs in the combination attack the cancer in a meaningful way. Finally, the Federal Court's

reference to the known "modest anti-cancer effects of PN" seems to indicate that it was satisfied both that (i) PN has some anti-cancer effect in the combination, and (ii) the degree of that anti-cancer effect from PN alone would be less than the patented combination (i.e. the combination offers better results than PN alone). This would seem to cover all of the essential elements of the claims in issue.

[46] Based on my understanding as described in the previous paragraph, I am not convinced that the Federal Court made any error on the issue of utility that was palpable or obvious.

[47] Apotex also challenges the relevance of the 004 Study because it gauged anti-cancer effects by means of PSA testing (which the Federal Court recognized, at paragraph 19 of the Reasons, was used as "a surrogate measurement for the effectiveness of prostate cancer treatments"), rather than a direct measurement. Apotex argues that a PSA result does not demonstrate utility; it merely provides a factual basis for a prediction of utility. Since Janssen cannot rely on a sound prediction of utility, Apotex argues, there is no proper basis for finding utility.

[48] I note first that the Federal Court found, as a fact, that PSA indicated the response to prostate cancer in 2007: Reasons, para. 19. This suggests that a reduced PSA level can be a demonstration of utility in fighting cancer.

[49] Moreover, it is not necessary that tests conclusively prove the requisite utility: Donald H. MacOdrum, *Fox on the Canadian Law of Patents*, 5th ed., s. 6:13(a); *Pfizer Canada Inc. v.*

Novopharm Limited, 2009 FC 638, 76 C.P.R. (4th) 83 at para. 87, aff'd 2010 FCA 242, 88 C.P.R. (4th) 405, rev'd on other grounds 2012 SCC 60, [2012] 3 S.C.R. 625. It is sufficient that the test results are strongly suggestive of utility, and that there is no other logical explanation for the test results is likely: *AstraZeneca Canada Inc. v. Mylan Pharmaceuticals ULC*, 2011 FC 1023, 96 C.P.R. (4th) 159 at para. 168, aff'd 2012 FCA 109, 101 C.P.R. (4th) 275. By this measure, PSA levels appear to be sufficient.

[50] More broadly however, it must be acknowledged that it is difficult to draw a clear line between a demonstration of utility and a prediction of utility. Professor Norman Siebrasse argues that there is no basis for distinguishing between the two in his article entitled "Must the Factual Basis for Sound Prediction be Disclosed in the Patent?" (2012) 28:1 C.I.P.R. 38. For the purposes of the present appeal, it is not necessary to address the question posed in the title of Prof. Siebrasse's article. However, I note the following observation at p. 47 thereof:

> This principled argument that there is no sharp distinction between demonstrated utility and sound prediction reflects the practical reality. Initially, researchers may start with a hunch or speculation that a particular compound is worth investigating to treat a certain disease. As more tests are carried out, the evidence gradually accumulates until that speculation may reasonably be termed a prediction. With more evidence, the prediction turns into a sound prediction. As even more evidence accumulates, the soundness of the prediction gradually increases, until there is a point at which one more piece of evidence is obtained, and the totality of the evidence suffices to establish demonstrated utility. In some cases there may be a particular trial or experiment that is so dramatic that a researcher might say, "Yesterday we could only predict, but today we know." In other cases the last piece of evidence may be no more significant on its own than anything that went before, and it is the cumulative weight of the evidence that establishes demonstrated utility.

[51] Bearing in mind the vagueness of the line between prediction and demonstration, the general agreement that a PSA level indicates response to prostate cancer treatment, and the

applicable standard of review, I would not intervene on the Federal Court's conclusion as regards utility.

D. *Infringement*

[52] Because the product that Apotex proposes to market, APO-ABIRATERONE, is AA only, and it is only at the time of administration that it is combined with PN to make the combination defined in the claims is issue, this appeal is not concerned with direct infringement. Apotex would not directly infringe the 422 Patent upon selling APO-ABIRATERONE. Instead, this appeal concerns whether Apotex's marketing of APO-ABIRATERONE would induce infringement. As often is the case in matters decided pursuant to the Regulations, the question of whether Apotex will induce infringement turns mainly on the content of the proposed product monograph for APO-ABIRATERONE (the Product Monograph) because this document indicates how Apotex proposes to market the drug.

[53] As indicated above, the parties agree that the applicable legal test for inducing infringement is found in *Corlac Inc. v. Weatherford Canada Inc.*, 2011 FCA 228, 204 A.C.W.S. (3d) 888 at para. 162:

> […] A determination of inducement requires the application of a three-prong test. First, the act of infringement must have been completed by the direct infringer. Second, the completion of the acts of infringement must be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place. Third, the influence must knowingly be exercised by the inducer, that is, the inducer knows that this influence will result in the completion of the act of infringement …

[54] The first prong (an act of direct infringement) will be satisfied when someone combines APO-ABIRATERONE with PN as proposed in the Product Monograph at the time of administration. Apotex argues that the Federal Court erred when it concluded that the Product Monograph was sufficient to satisfy the second prong of the test (influence to the point that, without it, direct infringement would not take place). It argues that infringement requires that both components of the claimed combination contribute meaningful anti-cancer effects, but the Product Monograph contemplates PN only for its palliative effects.

[55] I am not convinced that the distinction Apotex urges is valid. The key to the second prong of the test is the act that the Product Monograph induces. In this case, that is the combination of AA and PN for the treatment of CRPC. The Federal Court concluded that when that combination is administered, both the AA and the PN will contribute meaningful anti-cancer effects as contemplated in the 422 Patent. Therefore, the Product Monograph directs an act of direct infringement. Moreover, the inducement of the act of direct infringement by the Product Monograph will clearly be with Apotex's knowledge, thus satisfying the third and last prong of the test for inducing infringement. This is not a case, as sometimes happens, where both infringing and non-infringing outcomes can result from following the directions in the Product Monograph. In this case, following the Product Monograph will inevitably result in an act of infringement.

[56] Apotex argues that the Federal Court's analysis depends on the Indications and Clinical Use section of the Product Monograph, which directs the use of AA and PN to <u>treat</u> prostate cancer, and the meaning of "treat" therein being as flexible as in the 422 Patent. Apotex argues

that the Federal Court ignored expert evidence that the dosage of PN is not a therapeutically effective amount, in that it is insufficient to have an anti-cancer effect. However, the Federal Court noted that Apotex had admitted that PN has anti-cancer effects. Apotex argues that this reasoning was erroneous because the incidental anti-cancer effect of PN is irrelevant. However, this brings the argument full circle. The fact that an anti-cancer effect of PN may be incidental to its palliative effects does not alter the fact that direct infringement will inevitably result from the use of the combination as contemplated in the Product Monograph. Direct infringement occurs when all of the essential elements of the claimed invention are present, regardless of the infringer's knowledge of the patent or that the act in question will infringe. It is not in dispute that the Product Monograph states that "APO-ABIRATERONE (abiraterone acetate) is indicated in combination with prednisone for the treatment of metastatic prostate cancer (castration-resistant prostate cancer, mCRPC) in patients […]" This contemplates all of the essential elements of the patented combination.

[57] Apotex's inducement of the use of the infringing combination, together with its knowledge that its influence will result in the use of that combination, is sufficient to find inducing infringement. The issue of the anti-cancer effect being incidental does not assist Apotex because it is not necessary to establish that Apotex knew or intended that the combination would infringe. As I indicated at paragraph 45 of *Hospira*, "the knowledge at issue in the third prong of the test is knowledge that the influence is being exercised, rather than knowledge that the resulting activity will be an infringement."

[58] Infringement is a question of fact or mixed fact and law. Therefore, absent an extricable error of law, it is subject to review on a standard of palpable and overriding error. I see no such error in the Federal Court's analysis of infringement.

V. Conclusion

[59] Having concluded that none of Apotex's arguments concerning alleged errors by the Federal Court has merit, I would dismiss the present appeal with costs.

"George R. Locke"
J.A.

"I agree.
Wyman W. Webb J.A."

"I agree.
Richard Boivin J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

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