Federal Court of Appeal | Cour d'appel fédérale

Date: 20190125

Docket: A-288-17

Citation: 2019 FCA 16

CORAM: **WEBB J.A.**
BOIVIN J.A.
DE MONTIGNY J.A.

BETWEEN:

APOTEX INC.

Appellant

and

PFIZER CANADA INC., WYETH LLC and THE MINISTER OF HEALTH

Respondents

Heard at Ottawa, Ontario, on November 20, 2018.

Judgment delivered at Ottawa, Ontario, on January 25, 2019.

PUBLIC REASONS FOR JUDGMENT BY: BOIVIN J.A.

CONCURRED IN BY: WEBB J.A.
DE MONTIGNY J.A.

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PUBLIC REASONS FOR JUDGMENT

BOIVIN J.A.

I. Introduction

[1] On August 22, 2017, following proceedings under the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, Brown J. of the Federal Court (the Federal Court Judge) issued an order as part of his judgment (2017 FC 774) prohibiting the Minister of Health from

issuing a Notice of Compliance (NOC) to Apotex Inc. (Apotex) in respect of a Notice of Allegation (NOA) dated January 21, 2016 sent by Apotex to Pfizer Canada Inc., previously Wyeth LLC, (Pfizer or Wyeth) until the expiry of Canadian Patent No. 2,436,668 ('668 Patent). The '668 Patent concerns a drug called O-desmethyl-venlafaxine (ODV). It is used for the treatment of depression. This appeal relates to Form I ODV succinate which is a particular crystal form of a particular salt of ODV, namely ODV succinate.

[2] Apotex appeals the Federal Court Judge's decision. This appeal, along with the companion appeal in *Teva Canada Ltd. v. Pfizer Canada Inc. et al*. (2019 FCA 15), concern issues related to the Federal Court Judge's obviousness analysis in respect of the '668 Patent. These appeals did not proceed jointly and the hearings took place separately. A number of arguments advanced by Apotex and Teva against Pfizer nonetheless overlap as do, to some extent, these reasons and those forming part of the companion appeal decision.

[3] In essence, Apotex argues that the Federal Court Judge misconstrued and misapplied the test for obviousness as set out in *Apotex Inc. v. Sanofi-Synthelabo Canada Inc*., 2008 SCC 61, [2008] 3 S.C.R. 265 [*Sanofi*] and that his obviousness analysis is directly contrary to two judgments rendered by our Court: *Bristol-Myers Squibb Canada Co. v. Teva Canada Limited*, 2017 FCA 76, 146 C.P.R. (4th) 216 [*Atazanavir*]; and *Pfizer Limited v. Ratiopharm Inc.*, 2010 FCA 204, 87 C.P.R. (4th) 185 [*Amlodipine*]. Apotex also argues that the Federal Court Judge made palpable and overriding errors in considering the properties in his reasons because they are not part of the inventive concept and further erred in including certain elements of the invention story such as the work that occurred prior to the salt screen and after Wyeth first

discovered Form I ODV succinate. Apotex also contends that the Federal Court Judge erred in law by rejecting its evidence on anticipation and concluding that its allegations of anticipation were not justified.

[4] For the reasons below, I would dismiss the appeal with costs.

II. Federal Court Judge's decision

[5] The Federal Court Judge issued a decision spanning over 408 paragraphs. For purposes of this appeal, the following account of this decision is required.

[6] It is noted from the outset that the Federal Court Judge provided a thorough and comprehensive review of the facts and evidence submitted by the parties. This includes the invention story; the experimentation with ODV fumarate; the failed attempt to form a new drug of ODV; the attempt to form an acceptable salt of ODV; the screening of polymorphs and crystals; the evaluation of solubility of drug candidates; the preparation of ODV succinate; the permeability and bioavailability testing of the most promising ODV salt forms, including *in vitro* human cell-based Caco-2 assay and the *in vivo* rat perfusion test; the Beagle dog testing; and the Human testing and its subcontracting to SSCI, Inc. (SSCI).

[7] Against this background, the Federal Court Judge found that, on a balance of probabilities, Apotex' allegations of invalidity due to obviousness, inutility, anticipation, overpromising and double patenting together with Apotex' allegation of non-infringement were not justified. In reaching that conclusion, the Federal Court Judge discussed obviousness at

length, as this was one of the primary issues at first instance and is essentially the main issue in this appeal. The Federal Court Judge thoroughly reviewed the test for obviousness, reiterating and relying first and foremost on the Supreme Court's decision in *Sanofi*. In particular, the Federal Court Judge noted that *Sanofi* introduced the "obvious to try" test, but that in doing so, the Supreme Court directed that the "obvious to try" analysis should be approached cautiously (Reasons at paras. 206-208).

[8] The Federal Court Judge also recalled this Court's jurisprudence on obviousness rendered post *Sanofi*. He expressly referred to the recent decision of our Court in *Atazanavir* which not only reiterated that the innovative element of *Sanofi* was the introduction of the "obvious to try" test but also that the obviousness to try analysis is not meant to replace all previous inquiries and that other inquiries remain possible (Reasons at paras. 216-221).

[9] Having addressed the applicable principles of law, the Federal Court Judge undertook "step 1" of the obviousness analysis in accordance with the *Sanofi* framework. More particularly, after first identifying the notional skilled person in the art (skilled person), the Federal Court Judge discussed the common general knowledge of the skilled person. He noted that the common general knowledge would include the methods and techniques for salt and crystal formation, as well as knowledge of ODV as the active metabolite of venlafaxine and ODV as a free base and a fumarate salt (Reasons at para. 228). He further noted that, while the prior art disclosed ODV succinate as a potential salt, neither Form I ODV succinate nor any other crystal form of ODV succinate had ever been disclosed, made or characterized (Reasons at para. 229). As a result, the Federal Court Judge found that the skilled person could not predict whether or not a particular

salt formation experiment would result in stable crystals. Hence, the skilled person would not have known in advance whether ODV succinate generally, or Form I ODV succinate specifically, "would work" (Reasons at paras. 230-231). The Federal Court Judge also found that polymorph screening was not mechanical and repetitious work and that the skilled person would not be able to further predict before a polymorph screen "how many solid forms would [be] identified, what they would be, or what solid forms would result from any particular method or set of conditions." (Reasons at para. 232). The Federal Court Judge agreed with Pfizer that "there was no generally accepted procedure of selecting a salt form because each procedure is based upon the structure of each particular drug form." (Reasons at para. 240). He determined that the identification of crystals was not predictable and polymorph screening was seen as difficult, time-consuming and expensive (Reasons at paras. 243-244).

[10] The Federal Court Judge then turned to "step 2" in the obviousness analysis for purposes of defining the "inventive concept". He determined that the inventive concept of the relevant claims of the '668 Patent was the novel crystal form *i.e.*, Form I ODV succinate (Reasons at para. 249). This led to "step 3" of the obviousness analysis, whereby the Federal Court Judge concluded that the difference between the state of the art and the inventive concept of the relevant claims was "the invention of a new composition of matter namely Form I ODV succinate." (Reasons at para. 265).

[11] The Federal Court Judge's obviousness analysis subsequently turned to "step 4" *i.e.*, whether the differences between the state of the art and the inventive concept "constitute steps which would have been obvious to the person skilled in the art" or whether they require any

degree of invention. The Federal Court Judge first undertook this step by applying the pre-*Sanofi* definition of obviousness set out in *Beloit Canada Ltd. v. Valmet Oy*, (1986), 64 N.R. 287, 8 C.P.R. (3d) 289 (F.C.A.) [*Beloit*], namely whether the skilled person would have come directly and without difficulty to the solution taught by the '668 Patent, namely the novel crystalline Form I ODV succinate (Reasons at paras. 276-277 and 279). He found that the skilled person would have foreseen a difficult and indirect road ahead with a "large number of studies and tests with no predictable result" (Reasons at paras. 280-281).

[12] The Federal Court Judge then considered the "obvious to try" test and first determined that it was not "more or less self-evident that what is being tried ought to work". He acknowledged the cases cited by the parties but concluded that none of these cases indicated that all salt screens and all polymorph or crystal screens are obvious to try or are routine; rather, each case turned on its particular facts (Reasons at para. 289). In the present case and based on his review of the evidence provided by Pfizer's witnesses, Dr. Myerson and Dr. Park, the Federal Court Judge concluded that the skilled person could not predict that Form I ODV succinate existed, what properties it would have, or how it could be prepared, if at all (Reasons at para. 290).

[13] The Federal Court Judge also determined that, in the present case, there were not "a finite number of "identified predictable solutions" known to persons skilled in the art". Rather, the number of potential experiments "was in fact extreme (sic) large" (Reasons at para. 292). He explained that the knowledge of salt screens and polymorph tests merely provided avenues of research. The evidence demonstrated only "mere possibilities of identifying the ODV succinate

salt, or perhaps no salt at all, in a salt screen in first place, and a possibility of finding Form I ODV succinate crystalline, or perhaps no crystalline form at all, in crystallization and polymorph screening" and that "mere possibilities are not sufficient" (Reasons at paras. 296 and 298).

[14] The Federal Court Judge also considered the various elements of knowledge that Apotex asserted the skilled person would have and that would lead to the solution taught by the patent. The Federal Court Judge touched on each matter. In general, he concluded that "the fundamental problem with [Apotex'] arguments is that they are contrary to the expert evidence I have accepted" (Reasons at para. 301). Specifically, the Federal Court Judge observed that Apotex' arguments attested to the existence of the procedures rather than to whether it was more or less self-evident to try them (Reasons at para. 302).

[15] In addition, the Federal Court Judge concluded that "the extent, nature and amount of effort required to achieve the invention" was considerable (Reasons at para. 305). There was no evidence that the skilled person would have known which salt or crystalline form would achieve the invention. On the contrary, there was reason to believe that ODV succinate would not work because past experimentation with ODV fumarate had proved unsuccessful. ODV in its disassociated state (separated from the fumarate salt once dissolved) did not work when introduced into the body. The evidence therefore demonstrated that it was logical to expect that succinate salt also would not work "because the ODV dissociated from the succinate salt would be the same as the ODV dissociated from the fumarate salt." (Reasons at para. 306). In the words of the Federal Court Judge, the nature of the work was "uphill" (*ibid*).

[16] The Federal Court Judge also determined that while the salt screening alone may not be characterized as prolonged and arduous work, the invention story considered as a whole, including the pro-drug experiments and the SSCI polymorph and crystallization work, would be viewed as "prolonged and arduous" (Reasons at para. 308).

[17] As for the motive provided in the prior art, the Federal Court Judge affirmed the following:

> [311] There is no evidence of motivation in the prior art that points in the direction of the succinate salt of ODV, nor to any particular solid state form of ODV succinate, let alone the Form I monohydrate. This is not unexpected given the [s]killed [p]erson would have had no knowledge or predictability of what forms existed nor how they could be formed.

[18] The Federal Court Judge explained that while there may have been a motive to find a form of ODV that could be formulated, there was no evidence of motivation that suggested succinate salt as the solution (Reasons at para. 312).

[19] Finally, the Federal Court Judge examined the course of conduct which culminated in Form I ODV succinate. He concluded that this course of conduct in the context of the invention story which led to the making of Form I ODV succinate was not routine. Salt forms were seen as counter-intuitive and viewed with skepticism based on the past experience with ODV fumarate. More particularly, the Federal Court Judge indicated that five of the seven salts screened by Wyeth in the summer of 2000 could not be formed or were not crystalline. Moreover, work was performed prior to the salt screen, including the work with ODV fumarate and pro-drugs. Also, the considerable work conducted by Wyeth after the detailed salt and specialized crystal

polymorph screening could not be ignored (Reasons at paras. 318-319). Although some steps may not have been independently arduous, the Federal Court Judge was of the view that "viewed overall it was nonetheless difficult" (Reasons at para. 322).

[20] On the basis of the above, the Federal Court Judge concluded that Form I ODV succinate was not obvious or "obvious to try". Apotex' allegations were accordingly dismissed.

[21] With respect to Apotex' allegation of anticipation, the Federal Court Judge observed the "unusual manner" in which the issue came before the Court (Reasons at para. 369). Although Apotex raised anticipation in its NOA, Pfizer did not address the allegations of anticipation in its memorandum. At that time, Pfizer was of the opinion that anticipation was no longer before the Court because Apotex had not filed evidence regarding anticipation. However, when Apotex filed its memorandum, it became clear that anticipation was still at issue as it relied on the affidavit evidence of two of its experts with respect to obviousness to address the issue of anticipation and displace the statutory presumption of validity laid out in subsection 43(2) of the *Patent Act*, R.S.C. 1985, c. P-4.

[22] The Federal Court Judge rejected Apotex' expert affidavit evidence in this regard for several reasons:

A. neither expert was instructed on the law of anticipation and specifically on disclosure and enablement (Reasons at para. 373);

B. the evidence was tendered in respect of obviousness, not anticipation (Reasons at paras. 374-377); and

C. the parties should not be allowed "to imbed critical evidence on one issue into material filed in relation to another and different issue, and then, after all the

> evidence…is complete, rely on the imbedded evidence to attack the patent" (Reasons at para. 380).

[23] The Federal Court Judge also rejected Apotex' argument that its allegations of anticipation made in its NOA could be "evidence" to displace the statutory presumption (Reasons at para. 386). The Federal Court Judge equally determined that the International Patent Publication No. WO 851 (one of the prior patents disclosing ODV) did not assist Apotex' anticipation allegations as he had already determined that the prior art did not disclose Form I ODV succinate (Reasons at para. 387).

[24] In rejecting Apotex' anticipation allegations, the Federal Court Judge also determined that Pfizer could not lead evidence on anticipation and could only rely on the general presumption of validity. He held that "Pfizer may not split its case by declining to deal with the merits of an issue in its memorandum and then dealing with that issue in oral reply at the end of the hearing." (Reasons at para. 382).

[25] In conclusion, the Federal Court Judge concluded that the presumption of validity prevailed and that Apotex' allegations of anticipation were not justified.

[26] As mentioned above, the Federal Court Judge addressed other issues in his decision including claim construction, non-infringement, and utility but given that these issues are not subject to appeal they will not be addressed here.

III. Issues in this appeal

[27] The issues in this appeal are as follows:

- Did the Federal Court Judge err in concluding that Apotex' allegations of obviousness were not justified?
- Did the Federal Court Judge err in concluding that Apotex' allegations of anticipation were not justified?

IV. Standard of review

[28] Obviousness and anticipation are factual inquiries which involve questions of mixed fact and law. Hence, each case will turn on its own facts, and it is ultimately the role of the judge to apply the law to these facts. Absent an extricable legal error, the Federal Court Judge's application of the law to the facts is subject to the deferential standard of palpable and overriding error (*Housen v. Nikolaisen*, 2002 SCC 33; [2002] 2 S.C.R. 235 [*Housen*]; *Alcon Canada Inc. v. Actavis Pharma Company*, 2015 FCA 191, [2015] F.C.J. No. 1083 (QL) [*Alcon*]; and *ABB Technology AG v. Hyundai Heavy Industries Co., Ltd.*, 2015 FCA 181, [2015] F.C.J. No. 973 (QL)).

V. Analysis

A. *The applicable legal framework for obviousness*

[29] In this appeal, Apotex essentially contends that the Federal Court Judge made extricable errors of law in applying the test for obviousness and that he also made palpable and overriding

errors in his application of the test. Prior to addressing Apotex' contentions, it is apposite to recall the law on obviousness as it currently stands.

[30] The well-established framework for the obviousness inquiry remains the one set out by the Supreme Court in *Sanofi*. In that case, the Supreme Court established four steps (at para. 67):

1- Identify the notional "person skilled in the art" and the relevant common general knowledge of that person;

2- Identify the inventive concept of the claim or the claims in question;

3- Identify what differences exist between the "state of the art" and the inventive concept; and

4- Determine whether, viewed without knowledge of the alleged invention as claimed, those differences constitute steps which would have been obvious to the person skilled in the art or whether they require any degree of invention. In other words: Is the inventive concept obvious?

[31] In *Sanofi*, the Supreme Court also introduced at the fourth step the "obvious to try" test which lists a number of non-exhaustive factors to consider in determining whether the invention was "obvious to try" (*Sanofi* at para. 69). Although not every case will require an application of the "obvious to try" test, it can be appropriate in instances where the art in question encompasses advances made as a result of experimentation.

[32] Following *Sanofi*, our Court in *Atazanavir* echoed the Supreme Court's consideration of obviousness by reiterating that the "obvious to try" test must be approached with caution as it remains one factor amongst many that may assist in the obviousness inquiry (*Atazanavir* at para. 38; *Sanofi* at paras. 64-65). Our Court in *Atazanavir* explained that the "obvious to try" test

introduced by *Sanofi* had in no way displaced other tests, including the test set out in *Beloit*. Our Court expressly recalled that while the Supreme Court introduced the "obvious to try" test, it favours "an expansive and flexible approach that would include 'any secondary considerations that [will] prove instructive'" (*Atazanavir* at para. 61, referring to *Sanofi* at para. 63). As a result, a categorical approach to the obviousness inquiry and the elaboration of a "hard and fast rule" was specifically deemed inappropriate and rejected by our Court (*Atazanavir* at para. 62).

[33] With this in mind, I will now address the arguments put forward by Apotex as part of the present appeal.

B. *Did the Federal Court Judge err in applying the test for obviousness?*

(1) The application of the obviousness test by the Federal Court Judge

[34] Apotex contends that the Federal Court Judge made an error in his application of the obviousness test. As can be seen by the above-detailed account of the Federal Court Judge's decision, this contention is unfounded.

[35] Indeed, it is clear on the face of the Federal Court Judge's decision that he proceeded with his analysis of obviousness by using the four-step inquiry set out in *Sanofi*. Moreover, a review of the Federal Court Judge's decision shows that he fully considered the teachings of this Court in *Atazanavir* and properly applied *Beloit*. He also methodically considered whether or not the invention was "obvious to try". Specifically, the Federal Court Judge recognized that the "obvious to try" factors enumerated by the Supreme Court in *Sanofi* are not exhaustive and that

the “obvious to try” test is not a “panacea for alleged infringers” (Reasons at paras. 284-285; and *Sanofi* at para. 64). The Federal Court Judge’s application of the obviousness analytical framework was conducted in a thorough and considered manner and Apotex’ parsing of the Federal Court Judge’s analysis fails in showing any error on his part.

[36] In reality, Apotex is seeking to bring this Court to apply a correctness standard to the Federal Court Judge’s analysis on obviousness. Yet, absent an extricable question of law, it is well established that the standard of review to be applied for findings of fact or mixed fact and law is palpable and overriding error (*Housen*; *Alcon*). Furthermore, the Federal Court Judge is entitled to deference on his appreciation of the evidence, including the weight given to competing evidentiary submissions. It is not the role of this Court to reweigh the evidence put to him and to second-guess the Judge’s assessment of filed evidence (*Nova Chemicals Corporation* v. *Dow Chemical Company*, 2016 FCA 216, [2016] F.C.J. No. 995 (QL) at para. 14). In short, absent any palpable and overriding error by the Federal Court Judge, this Court ought not to interfere with his findings of fact or mixed fact and law.

(2) The Federal Court Judge’s consideration of properties in relation to the inventive concept

[37] Apotex does not contest that the inventive concept of the relevant claims is Form I ODV succinate. However, Apotex argues that the Federal Court Judge erred when he made reference to the properties of ODV succinate – and specifically Form I – in his reasons as they are not part of the inventive concept.

[38] In considering Apotex' argument, I am mindful that our Court cautioned in *Atazanavir* to not implicitly adopt a definition of the inventive concept that focuses on properties if the properties are not part of the inventive concept (*Atazanavir* at para. 74). However, in this case, the Federal Court Judge did not find non-obviousness on the basis that the properties were not predictable in the manner seemingly suggested by Apotex. Indeed, although the Federal Court Judge discusses properties in various parts of his reasons, his conclusion that Form I ODV succinate is not obvious does not rest solely on the unpredictability of the properties of a salt form. Rather, the Federal Court Judge relied on evidence that demonstrated that a skilled person could not have known or predicted that the Form I ODV succinate – *i.e.*, the crystal form itself – could be made or even existed:

> [229] However, Pfizer is correct in stating that while the prior art explicitly disclosed ODV as a free base and a fumarate salt, and ODV succinate as a potential salt, no crystal form of that salt let alone the crystalline Form I ODV succinate had ever been expressly disclosed, made or characterized. Also, none of the prior art teaches the successful preparation of a succinate salt of ODV nor does it teach, more importantly for this case, the successful preparation of Form I ODV succinate, and nothing in the prior art discloses any of the properties or [sic] either ODV succinate or Form I ODV succinate.
>
> [230] In my view, the number of experiments required to move from the acceptable pharmaceutical salts to the Form I ODV succinate was extremely large, as Dr. Myerson deposes at para 102 of his affidavit, and in the nature of a research program, not routine experimentation. Even though a [s]killed [p]erson may have had some general expectations about which salts may form, these expectations were theoretical and the evidence is that empirical testing was required to determine if a salt could be made and only then could its properties be assessed. It was impossible to predict in advance which of the many possible salts, if any, would have the most appropriate properties for formulation as a drug in terms of stability, solubility, permeability and bioavailability. Much the same was known in the prior art of crystals: the [s]killed [p]erson would know (sic) and could not predict which salt would crystallize, nor what properties the crystalline form, if any, would have. One would not know in advance that the succinate salt, or the crystalline Form I ODV succinate, in the language of the *Sanofi* test, "would work."

[39] Moreover, *Sanofi* and *Atazanavir* teach that the obviousness analysis must not be performed in a rigid way. On the contrary, it must proceed as part of a flexible, contextual, expansive and fact driven inquiry. Applying this principle to the present case, it was open to the Federal Court Judge to take the properties of the invention into consideration the way he did as part of his analysis. But more specifically, a fair reading of the Federal Court Judge's decision shows that his analysis is grounded in the fact that Form I ODV succinate itself is not obvious (Reasons at para. 303). As such, the references to properties in the Federal Court Judge's reasons provide relevant context in the present case as to whether the invention was obvious or obvious to try. Such references cannot sustain Apotex' contentions of error on the part of the Federal Court Judge.

(3) The Federal Court Judge's application of *Atazanavir* and *Amlodipine*

[40] Along the same lines, at hearing before our Court, Apotex argued that the Federal Court Judge also erred by failing to follow *Atazanavir* and *Amlodipine* because the fundamental facts in the present case are allegedly "indistinguishable" from those two cases and hence constitute binding jurisprudence. Had the Federal Court Judge followed *Atazanavir* and *Amlodipine*, says Apotex, he would have found its allegations of obviousness to be justified.

[41] Apotex' argument is misplaced. Indeed, prior to undertaking his detailed analysis of obviousness, the Federal Court Judge carefully considered a number of cases addressing the "obvious to try" test, namely *Atazanavir* but also *Apotex Inc. v. Pfizer Canada Inc.*, 2009 FCA 8, [2009] 4 F.C.R. 223; *Novartis Pharmaceuticals Canada Inc. v. Cobalt Pharmaceuticals Company*, 2013 FC 985, 440 F.T.R. 1; and *Eli Lilly Canada Inc. v. Mylan Pharmaceuticals*

ULC, [2015] FCA 286, 2015 F.C.J. No. 1463 (QL) (Reasons at paras. 211-222). There is no question that *Atazanavir* and *Amlodipine* as well as other past cases can provide helpful illustrations of the obviousness inquiry; however, contrary to what Apotex appears to urge, *Atazanavir* and *Amlodipine* cannot be used to force a given conclusion on obviousness based on broad factual similarities to the detriment of otherwise significant differences in a given case. However trite, each case is to be decided on the basis of the specific evidentiary record put before a judge.

[42] In the present case, the Federal Court Judge considered cases cited by the parties with the understanding that this jurisprudence does not establish any "hard and fast rules" on obviousness when it comes to evaluating whether or not a salt screen or any other form of experimentation is obvious or not:

> [289] … Both parties cited cases where, on the accepted evidence in a particular case, various courts came to conclusions on obvious to try. While of relevance, each case in this connection has been decided on facts particular to it, having regard to the submissions of the experts and counsel. Although Apotex pressed hard, it remains that none say that all salt screens are obvious to try, or involve only matters of routine experimentation. Nor do any say that all polymorph or crystal screen research is obvious to try or merely entails routine experimentation. None do and of course none could. Ultimately the proper characterization of each case is a question of applying the law of obvious to try as set out in *Sanofi* to the evidence before the Court.

[43] There are specific factual and evidentiary differences between both *Atazanavir* and *Amlodipine* and the present case which support the Federal Court Judge's finding on obviousness. These include the fact that in *Amlodipine* and *Atazanavir* the inventive concepts properly construed were salts whereby the inventive concept in the present case is a novel crystal form (Form I ODV succinate). Furthermore, in *Amlodipine*, the obviousness finding was based

on the fact that a "person skilled in the art would be motivated to test sulphonic acid salts in general and would have every reason to test the besylate salt as this had already been shown to offer advantages over other salts in terms of stability." (*Amlodipine* at para. 28). Also, in *Atazanavir*, it was uncontested that "the [s]killed [p]erson would have expected a salt screen to identify at least one salt with improved pharmaceutical properties over the free base: …" (*Atazanavir* at para. 7).

[44] In the present case, the Federal Court Judge determined that it was not predictable whether Form I ODV succinate could be prepared at all (Reasons at para. 290). He also noted that there was no motivation pointing toward ODV succinate, and that, in fact, there was reason to believe that ODV succinate would not work, or for that matter, any other salt as observed by the Federal Court Judge at paragraph 306 of his Reasons:

> Again by analogy to *Sanofi* at para 86, there is no evidence that at the relevant time a [s]killed [p]erson would know which salt, or which crystalline form, would work to achieve the invention *i.e.*, the crystalline Form I ODV succinate. In fact, in this case the evidence appears stronger than that in *Sanofi* against obviousness to try, because here there is evidence which I accept on a balance of probabilities that the salt ODV succinate in fact would *not* work. This evidence was based on the fact that ODV fumarate, another salt of ODV, had not worked. Because ODV in its dissociated state, *i.e.*, separated from the ODV fumarate salt once dissolved, did not work when introduced into the body, it was logical to expect that a different salt, namely ODV succinate, also would not work, because the ODV dissociated from the succinate salt would be the same as the ODV dissociated from the fumarate salt. If one did not work it was logical that that the other would now (sic) work... The nature of the work seen in this context was uphill.

[45] The above further demonstrates that the Federal Court Judge properly applied the analytical framework of obviousness set out in *Sanofi* as considered by our Court in *Atazanavir*. Apotex has failed to establish any reviewable error which would warrant our intervention.

(4) The Federal Court Judge's consideration of Wyeth's course of conduct

[46] Apotex asserts that the Judge should have only considered the salt and crystal experiments that directly led to the initial preparation of Form I ODV succinate and should not have considered Wyeth's broader course of conduct. Apotex puts forward two arguments in support of this contention.

[47] First, Apotex argues that the Federal Court Judge should not have considered as part of the "invention story" the work Wyeth completed before turning to the salt screen, including Wyeth's work with fumarate and pro-drugs. In this regard, it must be pointed out that in the 1990s, Wyeth was faced with the challenge of identifying a form of ODV that could be formulated into a drug. Studies were thus conducted on ODV fumarate, a salt form, but without convincing results as ODV fumarate exhibited poor oral bioavailability. In order to address the problem with ODV fumarate, Wyeth attempted to form a pro-drug with ODV which was unsuccessful (Reasons at paras. 44, 50-51).

[48] Apotex asserts that the work conducted with respect to fumarate and the failed pro-drug attempts should not be considered because "efforts in other directions [are] not relevant" (Apotex' Memorandum of Fact and Law at para. 57). Again, this assertion is misplaced. As part of the previously explained flexible, contextual, expansive and fact driven inquiry established by *Sanofi* and this Court's jurisprudence, it was open to the Federal Court Judge to consider the course of conduct of those involved in the claimed invention including the inventor and his or her team. The course of conduct factor can include a consideration of whether "time, money and

effort was expended in research looking for the result the invention ultimately provided before the inventor turned or was instructed to turn to search for the invention" (*Sanofi* at para. 71).

[49] Second, Apotex argues that the testing by SSCI is irrelevant because it occurred after Wyeth had initially prepared and identified Form I ODV succinate. Apotex further argues that in considering the additional testing by SSCI, which occurred after Wyeth had initially prepared and identified Form I ODV succinate, the Federal Court Judge "expanded" the gap between the inventive concept and the state of the art.

[50] The reality, however, is that identifying a stable crystal form was not the end of the process for Wyeth. Indeed, although Wyeth's objective was to develop the compound as a drug, the new crystal form still needed to be characterized. Moreover, Wyeth was unaware of whether other forms of ODV succinate could be made and whether their stability was sufficient to be used as a drug. In other words, Wyeth did not know "what they had". Wyeth thus considered it necessary to undertake a complete polymorph screen for ODV succinate and retained the specialized laboratory SSCI to conduct further analysis on the crystal sample. SSCI's testing occurred under a variety of conditions in order to attempt to identify as many different solid state forms as possible. The evidence accepted by the Federal Court Judge in this regard demonstrates that the creation and the analysis of a new solid state form flows from a detailed investigation. The Federal Court Judge concluded on the basis of the evidence that this was not a routine process and accepted the evidence of one of Pfizer's witnesses, Dr. Park, that "[c]onditions like the solvent(s) used, the temperature, the rate of cooling, the time course of the experiment and the presence of other reagents are all examples of things that can affect the solid state form of the

compound, if any, that is produced." (Reasons at para. 125 no. 34; see also, Reasons at para. 123). It is significant that the evidence provided by Dr. Park attests to the following (Reasons at para. 125 no. 36):

> The creation and analysis of new solid forms was not a rote process. It was not possible for us to predict at the outset how many solid forms we would be able to identify, what they would be, or what solid forms would result from any particular method or set of conditions. Therefore, this process often required numerous experiments and analyses, and strategy and judgment had to be employed in order to make decisions about how to proceed based on the results that we obtained.
>
> [Emphasis omitted]

[51] It is also noteworthy that in the course of the process of creating and identifying new solid state forms, SSCI discovered a new solid form that was not crystalline and identified several other crystalline forms (Reasons at paras. 132 and 137). Given the uncertainty in the circumstances surrounding the new crystal form identified by Wyeth, SSCI's empirical and extensive research work was in fact a continuation of Wyeth's work and was required in order to conclude that Form I ODV succinate was the most stable hydrated form. The Federal Court Judge's consideration of this was accordingly justified.

(5) The distinction between salts and crystals

[52] Finally, Apotex argues that the distinction between salts and crystals is a false distinction and that the present case does not concern crystal formation but rather concerns only salts and that it should therefore not be interpreted any differently from other "salt cases". Specifically, Apotex argues that crystals are obtained as part of salt screens and if the goal is to obtain crystals, this "only requires a good night sleep". It should be noted that this specific argument

was presented at the hearing by Apotex but not developed in its memorandum. To a certain extent, it overlaps with Apotex' argument to the effect that the Federal Court Judge erred in failing to apply former "salt cases", including *Atazanavir* and *Amlodipine*.

[53] A review of the evidence before the Federal Court Judge demonstrates that the characterization of crystal formation underlying this argument is not as simple and straightforward as Apotex puts it. Indeed, there was evidence before the Federal Court Judge provided by expert witnesses from both parties to the effect that the situation regarding crystals is a complex one. For instance, Dr. Steed, a witness for Apotex, confirmed that crystal structures are not predictable (Reasons at para. 243):

> The foregoing deals with the salts. The situation regarding crystals is, if anything more complex, and further from the capabilities of the unimaginative uninventive [s]killed [p]erson in my respectful view, based on the experience of Dr. Park which I have accepted and that of Dr. Myerson referred to at para 234 above. Apotex's witnesses confirm a number of points, a central one being the fact that identification of crystals was not predictable. Dr. Steed agreed that the [s]killed [p]erson in 2001 "cannot predict in advance how many crystal structures of a compound might be stable under a given set of conditions." … In 2009 he authored a book in which he stated that in general crystal structures are not predictable: … He confirmed that if crystal structures were generally unpredictable of [sic] 2009, they were also generally unpredictable to the [s]killed [p]erson as of 2001 …

[54] For his part, Dr. Myerson, an expert witness for Pfizer, provided similar evidence (Reasons at para. 234 no. 84):

> Nucleation of the initial crystal is unpredictable, and it is often difficult to crystallize a new synthesized compound for the first time. Once the initial crystal is obtained, it can be used to "seed" solutions to assist in further crystallisation of the compound. Under certain circumstances, the nucleation step can be delayed

> almost indefinitely. For example, a solution of phenyl salicylate can be kept at a liquid state for several years without any solid form emerging out of the solution.
>
> [Emphasis in the original]

[55] Once again, I am of the view that Apotex has not established any palpable and overriding error on the part of the Federal Court Judge. While a judge could come to a different conclusion in another case where a novel crystal forms part of the inventive concept, in the present case, the Federal Court Judge did not err in distinguishing between salts and crystals.

C. *Did the Federal Court Judge err in concluding that Apotex' allegations of anticipation were not justified?*

[56] It is trite that obviousness and anticipation call for different analyses. However, it is hard to see how one single piece of prior art could both disclose and enable Form 1 ODV succinate, when the Federal Court Judge has previously found that Apotex' allegedly anticipatory prior art references, taken together, do not render that crystal form obvious. Indeed, the only piece of the prior art that could possibly have disclosed the invention - *i.e.*, the WO 851 Patent - was expressly considered by the Federal Court Judge: "I have already discussed the WO 851 Patent, and found that as prior art it did not disclose the Form I ODV succinate" (Reasons at para. 387 and also at para. 300R). Accordingly, even if the evidence put forward by Apotex had been accepted by the Federal Court Judge, it would not have been sufficient to demonstrate that the invention had been anticipated.

VI. Conclusion

[57] In summary, the Federal Court Judge properly weighed the evidence before him in this case. In putting forward arguments based on a number of alleged reviewable errors, Apotex essentially attempted to convince this Court to reweigh and reassess the evidence. The Federal Court Judge was alive to the conflicting views of experts, preferred some over others and he provided fulsome reasons for doing so. His findings are deeply rooted in the evidence and the facts and ought not to be disturbed.

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

[59] These reasons may contain information subject to a Protective Order and are therefore being released on a confidential basis. Apotex and Pfizer shall have four days to jointly provide the Court with submissions as to the portions of the reasons that in their view must be redacted, failing which these reasons will become the public reasons and will be placed on the public file.

"Richard Boivin"

J.A.

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

"I agree
Yves de Montigny J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

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