Federal Court  Cour fédérale

Date: 20170922

Docket: T-1399-15

Citation: 2017 FC 777

Ottawa, Ontario, September 22, 2017

PRESENT: The Honourable Mr. Justice Brown

BETWEEN:

PFIZER CANADA INC. and WYETH LLC

Applicants

and

TEVA CANADA LIMITED and
THE MINISTER OF HEALTH

Respondents

PUBLIC JUDGMENT AND REASONS
(Original and Corrected Confidential Judgment and Reasons issued August 22, 2017)

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I. Nature of the Matter

[1] This is an application for an order pursuant to s 6 of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/1993-133 as amended, SOR/1998-166, SOR/1999-379, SOR/2006-242 [*NOC Regulations*] prohibiting the Minister of Health from issuing a Notice of Compliance [NOC] in respect of a Notice of Allegation [NOA] sent by Teva Canada Ltd., [Teva

or Respondent] to Pfizer Canada Inc., previously Wyeth LLC [Pfizer or Wyeth or Applicant], dated July 10, 2015, in respect of Canadian Patent No. 2,436,668 [668 Patent]. The 668 Patent covers the drug PRISTIQ, which is used for the treatment of depression.

[2] Teva alleges that Claims 8, 9, 33, 43 and 44 of the 668 Patent fail for obviousness and lack of utility. Teva also alleges that the 668 Patent is an invalid selection patent. While Teva raised non-infringement and anticipation in its NOA, it withdrew those allegations.

[3] Teva also withdrew, on the 3rd day of this 5 day NOC, its allegation that Pfizer obtained the 668 patent as a result of having made wilfully misleading statements in its patent application, *i.e.*, conduct tantamount to fraud, contrary to s 53 of the *Patent Act*, RSC 1985, c P-4.

II. Procedural Note

[4] As a procedural note, this case was argued before I heard argument in *Pfizer Canada Inc and Wyeth LLC v Apotex Inc and The Minister of Health*, in respect of which I will deliver reasons and judgment later today, 2017 FC 774. These two cases involve different NOAs filed by different second persons (Teva and Apotex), against the same first person (Pfizer) in respect of the same 688 Patent. While the invention story is essentially the same in both, the grounds of invalidity differ. The arguments were similar in some respects and differed in others; therefore there is repetition as between these two sets of reasons. The law is the same in both resulting in additional repetition.

[5] As guidance for those reading both decisions, I should note that while obviousness and inutility are raised in both proceedings, Teva did not argue non-infringement, anticipation or double patenting as Apotex did in its proceeding. The parties in this Teva proceeding agree on the constructions of Claims 8 and 9, but there was no agreement on claims construction in the Apotex proceeding. Apotex in its proceeding also raised overpromising arising out of subsection 27(3) of the *Patent Act* as a ground of invalidity, an argument that Teva did not advance in this case.

III. Summary of Conclusions

[6] In the reasons that follow I find on a balance of probabilities that Teva's allegations of invalidity due to obviousness and inutility are not justified. Therefore, Pfizer will have its Order of prohibition, together with costs on terms the parties have agreed upon.

IV. Facts

1. Witnesses

A. Pfizer

[7] **Dr. Syed Shah** is a former employee of Wyeth (and subsequently Pfizer) who has held a number of different titles at both companies. In the late 90s to early 2000s, he was the Associate Director of the Chemical and Pharmaceutical Development Department at Wyeth and was involved in the development of a suitable form of ODV for clinical research and commercialization. He oversaw the preclinical research conducted on ODV succinate (and other

forms of ODV), as well as later clinical research on ODV succinate and PRISTIQ. Dr. Shah is a named inventor on the 668 Patent. He was offered as a fact witness.

[8] **Dr. Allan Myerson** is a Professor of the Practice of Chemical Engineering at the Massachusetts Institute of Technology ("MIT"). He is an expert in crystallization and the crystallization of pharmaceutical solids. He was on the SSCI advisory board from 2001 to 2006. He previously provided evidence regarding the corresponding US patent.

[9] **Dr. Aeri Park** is a former Principal at SSCI, Inc., the research laboratory hired by Wyeth to conduct polymorph and crystal studies on ODV succinate. She managed the team of scientists who conducted the ODV succinate work, which included identifying, analyzing, and generating various solid state forms of ODV succinate. She is one of the named inventors on the 668 Patent. Dr. Park was offered as a fact witness.

[10] **Dr. Leonard Chyall** is the President of Chyall Pharmaceutical Consulting, LLC. He was formerly a Director at SSCI Inc. and had no direct involvement in the ODV succinate project. He trained under one of the inventors of the 668 Patent. He is an expert in solid state chemistry and has expertise in salt and polymorph screening and in the experimental and analytical techniques used to identify and characterize solid forms.

[11] **Dr. James Polli** is a Professor of Industrial Pharmacy and Pharmaceutics at the University of Maryland School of Pharmacy. His main research interests are (1) maximizing oral bioavailability through formulation and chemical approaches, and (2) developing public quality

standards for oral dosage forms. He is an expert in pharmaceutics, pharmacokinetics and bioavailability.

B. Teva

[12] **Dr. Fakhreddin Jamali** is a Professor in the Faculty of Pharmacy and Pharmaceutical Sciences at the University of Alberta. He teaches, researches and practices in the field of pharmacy and pharmaceutical sciences. He has expertise in clinical pharmacology, including matters of pharmacokinetics, bioavailability and bioequivalence.

[13] **Dr. Eugene F. Fiese** is a consultant with Fiese Pharmaceutics Consulting. Dr. Fiese is a pharmaceutical chemist expert in the areas of preformulation, pharmaceutics research and dosage form development.

[14] **Dr. Daniel Z. Lieberman** is a Professor of Psychiatry and Behavioral Sciences and Clinical Director at George Washington University. He is a clinician who teaches, researches and practices psychiatry and has particular expertise in the treatment of mood disorders including depression.

2. Background

[15] The 668 Patent concerns a drug called o-desmethyl-venlafaxine, henceforth referred to as ODV. ODV is a serotonin and norepinephrine reuptake inhibitor [SNRI] which is indicated for the treatment of depression. ODV works by simultaneously inhibiting the reuptake of both

serotonin and norepinephrine, which are two neurotransmitters believed to be implicated in depression and anxiety. The specific active pharmaceutical ingredient (API) at issue in this proceeding is Form I ODV succinate, which is a particular crystal form of a particular salt of ODV namely ODV succinate. Form I ODV succinate is a novel composition of matter, and is the subject of Claims 8 and 9, on which Claims 33, 43 and 44 depend. Pfizer argues and as will be seen, I have accepted that Form I ODV succinate is the subject of Claims 8 and 9, on which Claims 33, 43 and 44 depend.

[16] ODV is an active metabolite of ODV's parent drug, venlafaxine. ODV is called a metabolite because when venlafaxine is administered, it is chemically modified in the body to form ODV; it is ODV that is responsible for delivering some or all of the pharmacological effect.

[17] It is common ground that ODV itself and its use as an antidepressant have been known for some time. Venlafaxine had been previously approved to treat depression, and was marketed by Wyeth and now Pfizer, Wyeth's successor. Wyeth had ODV in hand since at least 1990. Wyeth marketed ODV, as the known metabolite of venlafaxine, under the names EFFEXOR and EFFEXOR XR. EFFEXOR is the immediate release version of venlafaxine (which converts in the body to ODV); EFFEXOR XR is the extended release version of venlafaxine (which also converts in the body to ODV). ODV is thus the API in both EFFEXOR and EFFEXOR XR.

[18] Both EFFEXOR and EFFEXOR XR contain venlafaxine hydrochloride which is a salt; venlafaxine hydrochloride is henceforth simply referred to as venlafaxine.

[19] ODV and "pharmaceutically acceptable salt forms thereof" were claimed in both US Patent No. 4,535,186 (US 186) Claim 22, issued in 1985, and in Canadian Patent No. 1,248,540 (CA 540), Claim 21, issued in 1989. CA 540 was granted to a predecessor company of the Applicant Wyeth, which predecessor company is also shown as an assignee of US 186.

[20] "Pharmaceutically acceptable salts" as the term is used in US 186 and CA 540, are made by reacting an acid and a base. ODV is a base; therefore, to make a salt an appropriate acid is required for such a reaction. Both US 186 and CA 540 claim ODV succinate as one of 11 "illustrative" pharmaceutically acceptable salts, and therefore include reference to reacting ODV with succinic acid. However, there is no suggestion that ODV succinate had ever been made, nor that a crystalline salt ODV succinate had ever been made, nor that Form I ODV succinate had ever been made it was made by Wyeth.

[21] In addition to disclosure in the Canadian (CA 540) and American (US 186) patents just mentioned, it is also agreed that another form of ODV, namely its free base *i.e.*, the drug ODV itself as opposed to a salt or crystalline form of the drug, was disclosed in International Patent Publication No. WO OO/59851 (WO 851) published in October 12, 2000. WO 851 listed 26 "pharmaceutically acceptable salts", again including succinic acid. Again there is no suggestion that ODV succinate had ever been made, nor that a crystalline salt ODV succinate had ever been made, nor that Form I ODV succinate had ever been made before it was made by Wyeth.

[22] The prior art disclosed that venlafaxine as EFFEXOR or EFFEXOR XR and their metabolite ODV were useful to treat depression.

[23] Depression is and was also well known to be serious medical condition that can be and is often debilitating to those who suffer from it. It is not disputed that all of these drugs including Form I ODV succinate help patients suffering from depression to regain and live more full and functional lives.

3. The Invention Story

[24] The essence of the inventive story is also not generally in dispute although aspects of it are; the parties disagree on its characterization, and how the inventive story relates to the obviousness and obvious to try and other principles in patent law. The inventive story is also relevant in the dispute over utility. In my view it warrants being set out in some detail; I will first summarize it and then set it out in more detail.

[25] The inventive story as I have found it is generally drawn from the affidavit of Dr. Shah who was at Wyeth at the time and who was in charge of commercializing ODV generally and then commercializing ODV succinate. The inventive story is also taken from the affidavit of Dr. Park who was in charge of polymorph screening of ODV succinate at a specialized company that performed polymorph screening for Wyeth, namely, SSCI, Inc. [SSCI].

[26] I accept the evidence of Dr. Park and Dr. Shah because they were there at the time of the invention, and have first-hand knowledge of the matters to which they depose. I appreciate that they are both named inventors on the 668 Patent, but am not persuaded this affected their evidence whether by affidavit or in cross-examination.

[27] Wyeth, now Pfizer, had venlafaxine and also knew that ODV was an active metabolite of venlafaxine. Wyeth through a predecessor company (together referred to as Wyeth) and Pfizer marketed venlafaxine as EFFEXOR and EFFEXOR XR. EFFEXOR delivered venlafaxine immediately, but for many patients it had to be administered several times a day. EFFEXOR XR, a sustained release version of EFFEXOR, could be delivered once a day; it delivered a larger dose at the outset but once inside the body its release was spread over a prolonged period of time. EFFEXOR XR is an extended or sustained release formulation which was better for many patients if not most patients, including those suffering depression, because taking a once-a-day pill was more convenient and led to greater compliance than taking multiple pills throughout the day. In addition, the extended or sustained release form would reduce side effects by reducing the amount of the drug released into the body at any one time versus EFFEXOR, the immediate release form of venlafaxine.

[28] Wyeth's problem with venlafaxine was that while its active metabolite was ODV, there was no solid-state form of ODV itself that could be safely stored, formulated into a drug, and effectively delivered to patients. Wyeth only had venlafaxine which relied on the body, and in particular on the liver, to be converted into ODV, venlafaxine's metabolite, which then acted as the anti-depressant in the body and more particularly in the brain.

[29] The new ODV drug which Wyeth sought to discover required several key characteristics: stability, solubility, permeability and bioavailability. Permeability is the ability of a drug to permeate through the lining of the GI tract. Bioavailability is the ability of a drug to get into the bloodstream, which in an oral dose involves permeating the GI tract.

[30] The searched-for new ODV drug had to be a stable, that is, it had to be a drug that could be stored safely throughout the manufacturing and distribution processes. The searched for ODV had to remain stable throughout these processes and also in the hands hospitals and patients over different ambient temperatures and humidity levels one would find in the places where it might be manufactured, stored, distributed, and or used.

[31] The searched-for drug had to be a drug that would dissolve in the gastrointestinal [GI] tract *i.e.*, a drug that was soluble. It also had to be a drug that would cross over from the GI tract into the bloodstream where it could do its work in the body's systems and in particular, in the brain, *i.e.*, it had to be a drug that was permeable and bioavailable.

[32] In addition to having stability, solubility, permeability and bioavailability, the searched for new ODV drug needed to have these qualities without unacceptable adverse side effects such as nausea and vomiting which were known issues with ODV.

[33] In summary, over some two years - with greatly increased activity towards the end - experimentation and drug development was conducted, initially by Wyeth, and then by Wyeth together with I consider a specialized contract laboratory, SSCI. Employees of both Wyeth and SSCI are named inventors on the 668 Patent.

[34] Wyeth and SSCI eventually identified a solid crystalline form of ODV that appeared to be stable, soluble and bioavailable. This crystalline form is known now as Form I ODV succinate, and Pfizer alleges this as the inventive concept in Claims 8 and 9 of the 668 Patent. It

is common ground that this crystalline form is a new composition of matter that was never made or disclosed before it was created by Wyeth.

[35] In this connection it is worth noting that while Teva alleged anticipation in its NOA, it subsequently withdrew that allegation. Therefore, in this proceeding it is not disputed that Form I ODV succinate is a "new" composition of matter per s 2 of the *Patent Act*'s definition of "invention."

[36] I referred to the experiments that Wyeth and SSCI conducted in which Wyeth created the crystalline Form I ODV succinate, and in which [redacted] In this connection, the experts agree that it would have been impossible for the Skilled Person to predict whether ODV succinate salt would form as a solid, whether that solid could be formed as a crystalline compound, or what the properties of any hypothetical crystalline solid would be in terms of stability, solubility, permeability and bioavailability and adverse effects; none of this would be known without conducting doing empirical research.

[37] As will be discussed further, in my view the extent of research envisioned by the Skilled Person and actually required in this connection was not routine, but in the nature of a research program. I wish to note that an issue in this proceeding is whether the experimentation involved was routine experimentation, and if so, what legal consequences flow from such a finding. This is because the work done by Wyeth included performing salt screening. The work done by SSCI entailed a different type of screening, known as polymorph or crystal screening. Pfizer and Teva

agree that in general terms both salt screens and polymorph screens were generally known to a person skilled in the art at the time (the Skilled Person).

[38] Wyeth not only created the Form I ODV succinate salt, but went further and discovered and created the new crystalline Form I ODV succinate claimed in Claims 8 and 9 of the 668 Patent. Wyeth however did not know that the crystal it created [redacted] SSCI found another three crystalline and one amorphous forms of ODV succinate in addition to crystalline Form I ODV succinate relied upon by Pfizer in Claims 8 and 9 of the 668 Patent.

[39] [redacted] This discovery allowed Wyeth to develop sustained release oral formulations that could deliver therapeutic concentrations of ODV over a prolonged period of time, reduce the overall incidence of certain side effects associated with higher peak blood concentrations of the drug, and give patients a once daily pill instead of having to take multiple pills throughout the day.

4. Invention story in more detail: the evidence of Pfizer's Dr. Shah

[40] Pfizer's Dr. Shah, a pharmaceutical engineer, was the lead investigator involved in Wyeth's development of ODV for clinical research and commercialization between 1999 and 2004. Dr. Shah's evidence was that at the outset of the course of Wyeth's experimentation, Wyeth's Discovery Group considered that ODV might be a successful drug candidate for several reasons. [redacted]

[redacted] For example, it was thought that by administering the metabolite ODV directly one could have a faster and more potent effect.

[41] In addition, it was known that individuals varied in their ability to metabolize venlafaxine into ODV in the liver, which would affect the effectiveness of venlafaxine. By getting rid of the metabolic step (in which venlafaxine is converted by the body into ODV) it was thought this variability could be addressed. [redacted]

[42] Wyeth was also interested in improving patient compliance, that is, improving the chances of patients actually taking the medication as prescribed, and potential to reduce side effects. One way to do this would be to develop a drug that could be dosed once per day, which meant developing a sustained release formulation of ODV.

[43] Wyeth's invention story had several components in addition to this background knowledge.

[44] Initially, Wyeth worked with ODV fumarate, a known salt form of ODV, but without success.

[45] Wyeth also attempted to make a pro-drug of ODV, again without success.

[46] In addition, and previously, Wyeth had worked with a number of other salt forms of ODV, but without success.

[47] Wyeth then set out to determine if it could identify a more appropriate salt form, a route in respect of which there was internal and science-based skepticism. Eventually Wyeth found the ODV succinate salt form, which it then with further research and experimentation, developed into a crystalline form then known as Form "A", which subsequently became known as Form I ODV succinate. Having identified positive properties of the crystal Form I ODV succinate in terms of solubility and stability, it engaged SSCI to test the crystalline Form I ODV succinate and identify and test for other crystalline forms; SSCI did so and identified three other crystalline forms of ODV succinate plus one amorphous form of ODV succinate.

[48] Wyeth conducted studies *in vivo* (in the body) in mice, and in cells *in vitro* (outside the body), together with *in vivo* tests on rats, beagle dogs and ultimately with human volunteers.

[49] Wyeth determined that the crystalline Form I ODV succinate had the requisite stability, together with solubility in addition to both suitable permeability and bioavailability. Wyeth then

performed additional studies to develop sustained release formulations of Form I ODV succinate. The following outlines these steps in more detail.

5. Experimentation with ODV fumarate

[50] Pre-clinical work on ODV by Wyeth's Discovery Group had been conducted on the fumarate salt form of ODV, known as ODV fumarate. ODV fumarate is formed by reacting ODV, which is a base, with fumaric acid to make a salt known as ODV fumarate. ODV fumarate is a salt form of ODV. ODV fumarate was a known salt form of ODV, which is one of the reasons it was looked at by Wyeth; as Teva notes, ODV fumarate was disclosed as Example 26 of US 186 as a crystalline salt.

[51] However, ODV fumarate had problems with bioavailability. [redacted]

[52] Teva disputes Pfizer's assertion that ODV fumarate was unsuitable because [redacted]

[redacted]

[53] This evidence indicates and I accept that oral bioavailability of ODV fumarate was relatively poor compared to ODV fumarate [redacted] The problem with the ODV fumarate's bioavailability was considered by Wyeth as "likely due to low solubility and/or permeability" of ODV fumarate. [redacted]

[54] [redacted]

[redacted], as Dr. Shah deposed in his affidavit, salts that are reasonably soluble like ODV fumarate are usually completely dissociated by the time they get to the GI tract. In other words, if the drug ODV became dissociated from its acid when it ceased to be a salt form in the GI tract, the same dissociation could obtain with other salts. Therefore if the dissociated drug ODV did not do well in terms of bioavailability when orally dosed as ODV fumarate, it was unclear why another salt form of ODV might behave better once dissociated from ODV itself:

Affidavit of Dr. Shah, para 22

[55] [redacted]

6. Attempt to form pro-drug of ODV

[56] Wyeth attempted to develop a pro-drug of ODV in 1999-2000. A pro-drug is a compound which is chemically altered in the body to become its bio-active chemical form. Pro-drugs are also described as being created by chemically modifying the active compound to produce a pharmacologically inactive molecule that will be metabolized into an active form in the body following absorption. Depending on the modifications that are made, the pro-drug may have improved solubility, dissolution or absorption over the active molecule.

[57] [redacted]

[58] [redacted] That said, I accept as a fact that Wyeth did pursue pro-drug development in relation to ODV.

7. Attempt to form an acceptable salt of ODV

[59] The third option contemplated by Wyeth (after the fumarate salt and pro-drugs) to improve ODV's absorption/permeability was to attempt to identify a new salt form of ODV. It was known that ODV existed as the salt form ODV fumarate as discussed above, but ODV fumarate was not pursued as such. It was also known that ODV existed as a free base, but ODV as a free base is insoluble in water which I accept leads to absorption issues; therefore the ODV free base was not pursued.

[60] I also accept that it was known, as indeed was stated by Dr. Shah, that salt formation provides a means of altering the physicochemical properties of a drug - like solubility and stability - without modifying its chemical structure. It is also accepted that salts are formed by interacting an acid and a base together to form a salt.

[61] ODV is a base. To attempt to make a salt with ODV, it was therefore necessary to interact ODV with an acceptable acid.

[62] [redacted] As a result, most of the pre-clinical work on ODV conducted by the Discovery Group was conducted on ODV fumarate, but as noted already, ODV fumarate displayed poor oral bioavailability.

[63] [redacted]

[64] [redacted], Dr. Shah proceeded to investigate other salt forms of ODV. This work began by his consulting Dr. Hadfield of Wyeth's Salt Selection Committee for assistance with preparing and screening new salts. [redacted]

[redacted]

[65] Dr. Shah and Dr. Hadfield started the salt screening process by preparing the [redacted] salt of ODV. [redacted]

[66] However, the hydrochloride salt of ODV displayed unfavorable properties for further drug development. [redacted]

[67] After discarding the [redacted] salt as a candidate, Wyeth continued to prepare other salt forms of ODV. Its goal was to identify salt forms of ODV that would exhibit a suitably low level of hygroscopicity, and display other properties necessary for development (such as crystallinity, aqueous solubility and stability). Dr. Shah stated that all of this was necessary before Wyeth could even get to the stage of testing permeability or bioavailability.

[68] Dr. Hadfield's lab notebook confirms that Wyeth attempted to prepare a number of different salts of ODV over the summer of 2000, including:

[redacted]

[69] In addition to these counter-ions, Wyeth tested additional salts in June and July of 2001.

[redacted]

[70] In addition, Wyeth also screened other types of salts following August 2000, [redacted]

[71] Teva notes that ODV succinate was one of the first salts identified after salt screening commenced; [redacted], as reported in para 68(e) above.

8. Polymorph and crystal screening

[72] Having identified these salts, the next step deposed to by Dr. Shah, who was present throughout these experiments as manager of commercialization of ODV, was to determine whether any the identified salts of ODV could be made as crystalline solids. Crystalline solids were preferable for development because they were often more stable and less hygroscopic than non-crystalline (amorphous) solids.

[73] [redacted]

[74] While crystallinity was highly desirable for a drug candidate, Dr. Shah's evidence, which I accept, was that not every crystalline salt would have suitable properties for drug development. Potential salts therefore also had to be evaluated for solubility, physical and chemical stability, and bioavailability. All of these properties are not necessarily found together in any one salt; for example, a salt that displayed good crystallinity and solubility may not have good physical stability (and vice versa).

[75] I therefore accept Dr. Shah's evidence that Wyeth was looking to develop the salt with the best combination of properties it could find. Because there was no way of predicting the characteristics of a salt at the outset, Dr. Shah's team continued to explore multiple candidates and screen further salts as other candidates advanced through solubility, stability and bioavailability testing. This allowed them to have alternative salt forms ready in the event that the leading salt forms displayed unfavorable properties in further testing.

9. Solubility

[76] After identifying these crystalline salts, Wyeth next evaluated the solubility of the potential drug candidates. The solubility of a drug candidate was important. In order for an oral dose of a drug to be absorbed in the GI tract, it had to have acceptable solubility to be in solution at the three sites of absorption (the stomach, the small intestine and the large intestine), each of which have different pH levels. Typically the pH of the stomach is 1.0, the pH of the small intestine is around 5.5, and the pH of the large intestine is around 7.0. This meant that the solubility of the salt had to be acceptable at each of these three pH levels.

[77] However, Wyeth was also looking for a drug candidate that could be administered once a day. Therefore, I accept that it did not want solubility to be too high, as this could cause the drug to be dissolved all at once and thus absorbed too quickly in the stomach; such rapid absorption would not be ideal for a once-a-day formulation as it might also cause nausea and emesis (vomiting) which had been exhibited with venlafaxine. Dr. Shah deposed that Wyeth was looking for a salt with solubility better than what was observed for ODV fumarate.

[78] In this connection, [redacted] The succinate salt was more soluble in my respectful view, which made it a likely candidate for further drug development.

10. The Preparation of ODV Succinate

[79] Given this, it is not surprising and the evidence I accept is that the crystalline salt form Wyeth chose for further evaluation was the succinate salt of ODV. [redacted] Once it was determined to form as a

solid, Dr. Hadfield attempted to induce it into a crystalline form, using a variety of solvents. [redacted]

[80] [redacted]

[81] [redacted]

[82] Dr. Shah's evidence which I accept was that ODV succinate monohydrate "appeared to have properties desirable for a drug candidate." As a result, it was promoted (along with some of the other salts of ODV that had been prepared) to permeability and bioavailability testing to see if it would fare better than the fumarate salt form.

11. Permeability and bioavailability testing

[83] Dr. Shah's evidence, which again I accept, was that the most promising ODV salt forms were tested in several bioavailability models, [redacted] and *in vivo* (in the body). His team's goal in conducting this bioavailability testing was to identify a form of ODV that would have sufficient permeability across the entire GI tract to best support once-a-day dosing.

[84] [redacted] permeability tests, [redacted] and the *in vivo* rat perfusion test, were initial keys to determining which salt, if any, might support once-a-day dosing.

[redacted]

[85] [redacted]

[86] [redacted]

13. Rat perfusion test

[87] A rat perfusion test is an *in vivo* (inside the body) test that directly measures the absorption properties of a compound in three regions of the GI tract of a rat: the duodenum-jejunum, the ileum, and the colon. I accept that this test was used by Wyeth because the literature established rat perfusion testing was a reliable predictor of a compound's absorption in the various regions of the human GI tract.

[88] Dr. Shah's evidence was that although it was most difficult to achieve permeability through the colon wall, absorption in the colon was desired to support once-a-day dosing.

[89] The rat perfusion tests involved injecting a solution of ODV succinate directly into clamped off sections of the GI tract of male rats (the duodenum, jejunum, ileum and colon). The rats were anesthetized and small segments of their GI tracts were surgically isolated for this permeability testing. The concentration of ODV succinate was measured at each time point using a known analytical technique. The difference in concentration between the inflow and the outflow represented the amount of drug absorbed by that segment of the GI tract over that period of time.

[90] [redacted]

[91] The results of the rat perfusion assay are reported in terms of “Peff” values. Peff value is the rate of perfusion (in cm/sec) of the drug across the intestinal wall.

[92] From the Peff value the evidence is that one may calculate, using a known equation, the predicted amount of the drug that would be absorbed through the human GI tract. This calculation results in a “Fa” value (“fraction absorbed”), which is the percentage of the drug present reliably predicted to be absorbed in the human GI tract.

[93] The results of [redacted] rat perfusion test were surprising in terms of the permeability of ODV succinate. [redacted], ODV succinate was more permeable than ODV fumarate; ODV fumarate was significantly less permeable than ODV succinate in all tested GI segments. Moreover, ODV fumarate had both Peff and therefore Fa values lower than ODV succinate in all three regions.

[94] Importantly given Dr. Shah's evidence concerning absorption in the colon, while ODV fumarate showed no absorption in the colon, ODV succinate was permeable throughout the GI tract including the colon. Indeed, it had a Fa value of 16% in the colon (compared with 0% for ODV fumarate).

[95] This result was surprising because, as Dr. Shah had explained earlier, it was not expected that any difference in solubility between the two salts would be a factor in the extent of their permeabilities. Since both salt forms were completely soluble at the concentration used for each experiment, the ODV cation (the ion with a net positive charge in solution) would have been anticipated to be dissociated from its fumarate or succinate anion (the ion with a negative charge in solution). In both experiments, the ODV cation should have been able to diffuse through the wall of the GI segment without any significant impact from the anion (because in solution the two counter ions are kept separated by water molecules).

[96] To Dr. Shah's knowledge, which I accept, [redacted] His evidence was also that although ODV succinate certainly had higher solubility (which can be one factor that

contributes to GI perfusion), ODV fumarate would have been expected to behave similarly to ODV succinate. He deposed that [redacted]

[97] Teva's expert Dr. Fiese, infers that because the fumarate salt went to rat perfusion studies it [redacted] However, Dr. Shah could not recall if this was the case; Dr. Shah deposed in his reply affidavit that to his knowledge the records are not available. Dr. Shah further deposed in his reply to this inference by Dr. Fiese, that [redacted] I accept Dr. Shah's evidence that ODV fumarate was a natural reference salt for permeability testing of novel salt forms, which included [redacted] the rat perfusion *in vivo* tests.

[98] Moreover as deposed Dr. Shah, the purpose of Wyeth's permeability testing was to try and improve upon issues observed with the ODV fumarate. [redacted]

[99] I am not persuaded by Dr. Fiese's inference in this respect. With respect, I accept Dr. Shah's explanation for two reasons: he was present at the time and his explanation makes sense. I accept the evidence of Dr. Shah over the speculation of Dr. Fiese.

14. Beagle dog testing

[100] Having observed and documented ODV succinate's superior solubility together with its improved permeability over ODV fumarate in the rat perfusion tests, and the relatively poor bioavailability of ODV fumarate observed in mice, Wyeth moved on to determine whether ODV succinate would have suitable bioavailability in another reliable *in vivo* system used for testing drug development, namely beagle dogs. Dr. Shah's evidence which I accept, was that "[B]ased on its superior solubility and permeability characteristics, we expected that ODV succinate would have improved bioavailability over ODV fumarate and would be appropriate for a once a day, extended release formulation. It was therefore selected for further development."

[101] Thus ODV succinate was advanced to *in vivo* beagle dog tests. However, the fumarate salt was not subject to beagle dog testing. Teva criticizes the fact that Wyeth did not test ODV fumarate in beagle dogs, but in the circumstances that decision is not objectionable because Wyeth had already established that the ODV fumarate had poor bioavailability.

[102] In the beagle dog testing, Dr. Shah's evidence, which I accept, was that Wyeth was looking for an oral dosage forms of ODV succinate to administer to the dogs to evaluate oral bioavailability. As part of the development efforts, Wyeth had started experimenting with different formulations of ODV succinate (*i.e.*, different combinations of ingredients mixed with

ODV succinate to produce solid dosage forms, like tablets). In particular, in accordance with its goal of achieving once-a-day dosing, Wyeth was already working on developing an oral sustained release formulation of ODV succinate.

[103] The beagle dog test was conducted using several different ODV succinate formulations, including intravenous, oral solution plus two other oral formulations: a capsule designed for immediate release, and a tablet designed for sustained release. The tests proceeded in four stages. In each stage, the beagles received one of the four different formulations of ODV succinate. Blood was taken from the dogs at specified intervals during each stage and was separated, frozen and shipped once again to Wyeth's Gosport facility in the United Kingdom for analysis. The concentrations of ODV present in the blood were determined by accepted methods and a number of pharmacokinetic parameters were calculated.

[104] The results of the beagle dog bioavailability testing are summarized in [redacted] a table summarizing the mean data from all six dogs as a function of the concentration of free ODV in the blood. The pharmacokinetic parameters reported in the table include:

(a) AUC ("area under the curve") - which measures the total amount of ODV present in the blood over the time course of the experiment;

(b) Cmax - which measures the peak plasma concentration of ODV;

(c) tmax - which measures the time at which peak concentration occurs; and

(d) absolute bioavailability-which measures the amount of ODV (as a percentage of the dose administered) found in the plasma.

[105] [redacted]

[106] The conclusion of this beagle dog testing, which I accept, is that the oral bioavailability of ODV succinate in beagle dogs fell within an acceptable range in all formulations tested.

15. Human Testing

[107] With the [redacted] *in vivo* testing in rats and beagle dogs showing positive results, Wyeth moved to testing with 18 human volunteers. Teva questions the fact that these test subjects were not patients suffering from depression. However, I am not persuaded this objection has merit because the human tests were not designed to test the efficacy of the ODV succinate drug in humans, but instead to assess bioavailability and side effects. It was also already known that ODV as the metabolite of venlafaxine, commercialized previously and sold as EFFEXOR and EFFEXOR XR, was useful in treating depression.

[108] Wyeth's human *in vivo* oral bioavailability studies of ODV succinate were conducted by comparing immediate release and sustained release formulations of the ODV succinate salt, against Wyeth's already successfully commercialized sustained release venlafaxine product EFFEXOR XR.

[109] As in Wyeth's *in vivo* beagle dog studies, its human study ran in three stages. In each stage each of the 18 human participants were given 75 mg of EFFEXOR XR as the comparator to the IR and SR formulations of ODV. Blood samples were taken at specific time periods in each stage and the concentrations of venlafaxine and ODV in the blood were measured. A number of the same pharmacokinetic parameters were calculated (AUC, Cmax, tmax) as well as t 1/2 (which measures the amount of time it takes for half of the drug to be eliminated from the plasma). [redacted]

[110] The results of the human studies are summarized [redacted] Again, Wyeth noted that oral bioavailability was good in both the immediate and sustained release formulations of ODV succinate. However, the sustained release formulation of ODV succinate resulted in peak plasma concentrations that were lower, and the time to maximal concentration was longer, than observed with the immediate release formulation.

[111] The human study was also designed to observe side effects of [redacted] and ODV succinate. Dr. Shah deposed that while conducting the human studies, Wyeth noted the reports of adverse events or side effects experienced with the various formulations. Wyeth was interested in monitoring several common adverse events (such as nausea, vomiting,

etc.) because they were frequently reported with the use of EFFEXOR. Wyeth noticed that the reported adverse events were lower with the sustained release formulation of ODV succinate than with the immediate release formulation - a fact I accept. Wyeth considered that this was likely due to the lowered peak plasma concentration (Cmax) and delayed time to peak plasma concentration (tmax) achieved with the sustained release formulation.

[112] Based on its data, Wyeth concluded that sustained release formulation of ODV succinate which resulted in peak plasma concentrations of less than 225 ng/mL (the lower end of the range observed for the immediate release formulation) would result in a reduction of these side effects.

[redacted]

[113] Dr. Shah deposed, and I accept, that from this human *in vivo* testing, as a flattened blood plasma concentration to time profile was achieved, adverse events were reduced or eliminated. Thus, a pharmaceutical composition comprising a sustained release formulation of ODV succinate having a peak blood plasma profile of less than about 225 ng/ml with reduced side effects such as nausea and emesis (vomiting) had been achieved.

[114] The evidence is and I find that the lower end of the range observed for the immediate release formulation, as deposed to by Dr. Shah, namely 225 ng/ml, is the derived result of the human subject testing which showed that the Cmax of the IR form of ODV succinate was 287 plus or minus 52, such that the lower end of the range was 225 ng/ml; this is the result disclosed

on page 53 of the 668 Patent. I am unable to accept Teva's argument that this concentration is arbitrary.

[115] I also find that the sustained release version of ODV succinate showed considerably lower adverse side effects when compared to the immediate release version of ODV succinate. Of the 18 subjects given the immediate release single dose of ODV succinate, 10 and 6 reported nausea, 2 vomiting, 1 diarrhea, 1 abdominal pain, 2 headache, 2 vaso-vagal malaise and 1 reported trismus. There were only 2 reports of nausea with the sustained release version of ODV succinate and 1 of abdominal pain; none of the human test subjects reported any other adverse side effect noted with the immediate release dosage. Dr. Shah properly noted in his affidavit that the report at page 54 of the 668 Patent, through a typographical error, reported no reports of abdominal pain with either the immediate or sustained release versions of ODV succinate when in fact there was 1 report for each: this error is not material to the improvement in side effects of the sustained version over the intermediate release version.

16. Solid state forms: crystallinity, amorphous solids, polymorphs

[116] Dr. Shah's evidence which again I accept was that one criterion for a viable drug form was a candidate that could exist as a crystal, or "exhibit crystallinity." Crystallinity refers to the organization of the molecules in a drug compound (or salt) in three-dimensional space. In a crystalline solid, the molecules making up the substance are organized in repeating patterns. By contrast, non-crystalline solids (often referred to as "amorphous" solids) have molecules that are randomly arranged. Crystalline solids were preferable for pharmaceutical drug form development because they were typically more stable than amorphous solids.

[117] Further, Dr. Shah deposed, and I accept that some compounds may exist in more than one solid-state form, which may include amorphous forms and/or one or more crystalline forms. Different crystalline forms of the same compound are usually referred to as "polymorphs." Dr. Shah and his group understood that different polymorphs of the same compound could have very different physical properties (such as solubility, melting point and stability), and that these properties could be relevant to drug form development.

17. Polymorph screening and subcontracting polymorph screening to SSCI

[118] As outlined above, when conducting preliminary screening of ODV succinate for crystallinity, Dr. Shah and Wyeth's Dr. Hadfield created a stable and soluble crystalline monohydrate form. However, in order to ultimately develop the compound as a drug, Dr. Shah's evidence which I accept was that it was important to have a stable and reproducible solid form that would not be susceptible to degradation or conversion during storage under different humidity conditions at room temperature and during the manufacturing and distribution processes. Therefore, to have a better idea of the range of possible solid state forms for a given salt, and to determine their individual properties, as well as for possible regulatory compliance, Wyeth considered it necessary to undertake a complete polymorph screen for ODV succinate.

[119] I accept Dr. Shah's evidence that a polymorph screen is a process of discovering further unknown crystal forms of a substance by exposing the substance to a number of different solvents and conditions, and subsequently characterizing the resulting forms (whether crystalline or amorphous). Through this process the drug commercialization developers could get an idea of what the various crystal forms of a compound might be, and under what conditions they may be

expected to form. Dr. Shah added that this process is labour intensive and often involves many individual experiments, and that [redacted]

[120] [redacted] Because finding a stable solid form that could be consistently prepared was very important to further development, for this reason also Wyeth determined that a detailed investigation of the solid forms of ODV succinate was necessary to define possible crystal forms.

[121] As a result, Wyeth retained an outside scientific consulting group, SSCI to conduct a detailed polymorph screen of ODV succinate. Wyeth asked SSCI to:

[redacted]

[122] [redacted]

[redacted] I will consider these arguments as part of the obvious to try analysis later in these reasons.

[123] As a result of its work, SSCI identified and characterized four crystal forms of ODV succinate as well as one amorphous form; three of the crystal forms SSCI identified for the first time, the fourth was the crystal form developed by Wyeth and given to SSCI for its work.

[124] [redacted] Dr. Shah concluded [redacted] that one particular crystal form of ODV succinate monohydrate [redacted], but which is now known and described in the 668 Patent as Form I ODV succinate) [redacted] could be expected to be stable under the conditions required for manufacturing and storage. This, combined with the other favorable properties of ODV succinate, made Form I ODV succinate a very attractive candidate for development as a drug. I now turn to SSCI'S involvement.

18. Dr. Aeri Park at SSCI

[125] The person managing the team of scientists conducting SSCI's work on ODV succinate was Dr. Aeri Park. Dr. Park studied and worked in the field of chemistry for 30 years, and has worked specifically in the area of drug development and characterization for 20 years. She began working as a Technician for SSCI in 1998 and was promoted to the role of Scientist that same year. She was promoted to Senior Scientist in 1999, to Senior Research Investigator in 2000, and to Director in 2001. As a Director, she was responsible for managing multiple teams of scientists working on solid state chemistry projects, interacting with clients and identifying new

approaches and potential routes of analysis for our projects. She was also responsible for providing training to new scientists on how to use the wide range of instrumentation and laboratory tools at SSCI's laboratory. Her involvement with the ODV succinate project began in 2001, when Wyeth retained SSCI to conduct a complete polymorph screen of ODV succinate.

[126] I accept Dr. Park's evidence of what SSCI did because of her experience and personal involvement with this particular compound and relevant knowledge of work in this area. She oversaw the work conducted by the scientists primarily responsible for carrying out the day-to-day experimentation on the ODV succinate project; these scientists reported directly to her. Dr. Park is one of the named inventors on the 668 Patent but I am not persuaded this affected her evidence in any way.

[127] [redacted]

[128] [redacted]

[redacted] Dr. Park deposed, and I accept, that SSCI's goal was to try as many different conditions as possible, because different conditions could produce different polymorphs and pseudo-polymorphs. Conditions like the solvents used, temperature, rate of cooling, time course, the experiment and the presence of other reagents are all examples of matters that may affect the solid state form of the compound. Therefore, Dr. Park deposed and based on her personal experience I accept that SSCI typically conducted a large number of different experiments under a wide variety of conditions in order to try to identify as many different solid state forms as possible.

[129] Dr. Park's evidence based on her experience was that the creation and analysis of new solid state forms in not a rote process. Having carried out or supervised some 10 to 20 polymorph screens per year during her tenure at SSCI, I accept her expert evidence on polymorph screens generally; by the times in issue she would have carried out or supervised 10 to 20 or more polymorph screens. Her evidence was as follows:

> **Polymorph Screens**
>
> 20. I carried out or supervised approximately 10-20 polymorph screens per year during my tenure at SSCI. Screens typically took three to four months to complete but he timing depended on the project, the sample and the goals of the client.
>
> 21. Screens broadly followed the frame-work of answering the questions identified in the ICH Q6A, a guideline developed by the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. <u>While each polymorph screen generally followed this same broad framework – such as starting by identifying the solid state forms of the provided sample and then carrying out a range of experiments to attempt to generate additional solid samples – each screening</u>

project was different. For example, in one screen we might discover only one crystalline form, whereas in another we might find many. In yet another scenario, we might not be able to generate crystalline material at all. The duration, direction, results and steps to be taken in each project depended on the characteristics of the compound being studied and the goals of our client.

22. At regular intervals throughout the screening project, I would discuss the experimental results to date with the members of my team, and we would decide on what additional experiments and analyses to conduct, in light of the results obtained thus far. The end goal was usually, but not always, to identify the most stable solid state crystal form of the sample provided, but this was not always possible.

[Emphasis added.]

[130] Dr. Park deposed that:

Generating Solid Samples

31. Our goal in generating solid samples was to try as many different conditions as possible because different conditions could produce different polymorphs and pseudo-polymorphs of the compound. Conditions 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. Therefore, we would typically conduct a large number of different experiments under a wide variety of conditions in order to try to identify as many different solid state forms as possible.

32. There were several different methods that we could use to try to generate different solid state forms from solution. These were, generally speaking, divided into methods involving thermodynamic conditions and methods involving kinetic conditions. [redacted]

[redacted]

33. 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 added.]

[131] Dr. Park detailed the process SSCI followed in identifying and creating new crystal and amorphous forms in her affidavit, which I accept as outlined below:

Characterization of Initial Solid Samples

39. [redacted]

40. [redacted]

41. [redacted]

[redacted]

42. [redacted]

43. [redacted]

44. [redacted]

45. [redacted]

46. [redacted]

[redacted]

47. [redacted]

48. [redacted]

Other Techniques for Analysis and Characterization

49. [redacted]

50. [redacted]

[Emphasis added.]

[132] [redacted]

[133]

20. Melting points and differential scanning calorimetry (DSC)

[134] , SSCI also conducted DSC analyses on the crystal forms in order to determine the temperatures at which phase transitions (like melting) occurred. DSC is a technique of measuring a melting event. Based on these analyses, the melting point of

Form “A” was determined to be about 131 °C (endothermic maximum) and the melting point of Form “B” was determined to be about 127 °C (endothermic maximum). The DSC data did not show any dehydration event but showed a single melting event which showed that water molecules were very strongly bound in the crystalline lattices of Form “A” and Form “B”‘. This was consistent with the TGA data, where the loss of water did not occur past 100 °C. Hydrates tend to lose the water of crystallization fairly readily at elevated temperatures due to dehydration, and convert to anhydrous crystalline forms or non-crystalline material.

[135] Therefore, the DSC [redacted] data indicated that Forms “A” and “B” are very stable hydrates. [redacted]

21. Further temperature studies and amorphous form

[136] [redacted] One of the additional tests that they performed during this time was variable temperature XRPD (VT-XRPD), which involved running XRPD analyses over a range of temperatures to check for changes in the resulting diffractograms. Using this test they could observe whether or not the crystal form was stable to changes in temperature or whether it would change or convert to another form. [redacted]

[137] During these studies they also identified an amorphous (non-crystalline) form of ODV succinate

22. Hygroscopicity testing (a test relevant to drug statbility)

[138]

[139]

24. (Crystal Form “C”)

[140])

[141] SSCI thereby identified crystal Forms “A”, “B” and “C”, and then identified crystal form “D” through

25. (Crystal Form “D”)

[142]

[redacted]

[143] [redacted]

[144] In the result, SSCI identified four polymorph forms of ODV succinate, namely Forms "A", "B", "C" and "D". Of these Form "A" was discovered by Wyeth; Wyeth provided Form "A" to SSCI. Therefore, SSCI succeeded in identifying three new crystalline forms of ODV succinate, plus one new amorphous form. In all, five forms of ODV succinate were identified by SSCI, four for the first time.

[145] [redacted]

[146] In essence, while Wyeth's Dr. Hadfield had identified ODV succinate as a salt and had also identified a crystal form, SSCI after thoroughly exploring the field, had determined there were three other crystalline forms of ODV succinate plus one new amorphous form.

26. Work on other salt candidates and screens

[147] Notwithstanding Wyeth and SSCI had made a new composition of matter namely Form I ODV succinate in a crystalline form, Dr. Shah's evidence, which I accept, was that

[148]

[redacted]

[149] [redacted]

V. Issues

[150] As noted previously, while Teva alleged non-infringement and anticipation in its NOA, it subsequently withdrew these issues. Mid-hearing Teva also withdrew its allegation that the 668 Patent was obtained contrary to s 53 of the *Patent Act* by "material" "untrue" allegations in the 668 Patent [henceforth, misleading statements].

[151] Therefore, the only issues remaining are obviousness and lack of utility, giving rise to the following two issues:

1. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Teva's allegation of obviousness is not justified.

2. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Teva's allegation of lack of utility is not justified.

VI. Statutory provisions and burden of proof

[152] Pursuant to s 2 of the *Patent Act*, to be patented, an invention must be "useful." Further, a new and useful "composition of matter" such as Pfizer claims here, may be patented:

invention means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter; *(invention)* [Emphasis added.]	***invention*** Toute réalisation, tout procédé, toute machine, fabrication ou composition de matières, ainsi que tout perfectionnement de l'un d'eux, présentant le caractère de la nouveauté et de l'utilité. *(invention)* [Soulignements ajoutés.]

[153] In *Novartis Pharmaceuticals Canada Inc v Cobalt Pharmaceuticals Company*, 2013 FC 985 [*Novartis*], Justice Hughes said the following regarding the burden of proof applicable in cases where a patent's validity is challenged in an NOC proceeding:

> [23] Who bears the burden when validity of a patent is at issue in NOC proceedings has been discussed many times in this Court. In brief: a patent is presumed to be valid in the absence of evidence to the contrary (*Patent Act*, s. 43(2)). The party alleging invalidity (here Cobalt) has the burden of putting forth evidence supporting its allegations. Once evidence is led the matter is determined by the Court on the civil burden of proof; namely, balance of probabilities. If the Court finds the matter to be evenly balanced, then it should find in favour of the person alleging invalidity since, under the *NOC Regulations*, subsection 6(2), the first person (here Novartis) bears the burden of demonstrating that the allegations of invalidity are not justified.

VII. Analysis

1. Relevant Dates

[154] The relevant dates are mostly agreed upon:

- Filing date in Canada: February 11, 2002, claiming priority to two previous applications, dated February 12, 2001 and June 13, 2001;
- Publication date: August 22, 2002;
- Issuance date: May 26, 2009.

[155] The relevant date for assessing obviousness is February 12, 2001.

[156] The parties agree that relevant date for assessing utility (whether demonstrated or soundly predicted) is the Canadian filing date: February 11, 2002. However, Pfizer denies that information that post-dates this date is relevant to Teva's allegations that the utility requirements of the *Patent Act* have not been met. Teva on the other hand, does not agree that information that post-dates the Canadian filing date is irrelevant, taking the position that if a sound prediction has subsequently been shown to be wrong, the patent would be invalid for want of utility. Such inutility, says Teva, can be proven at a later time. These arguments were made before the Supreme Court ruled in Promise Doctrine was not to be followed. Teva also says that a selection patent is invalid if further research reveals that a larger number of unselected compounds possess the same advantage as that claimed in the selection; I do not need to consider this dispute because I have the 668 Patent is not a selection patent.

[157] The 668 Patent is to be construed from the perspective of a person of ordinary skill in the art as of the date of publication: August 22, 2002.

[158] This application was commenced on August 24, 2015, therefore the 24 month stay imposed by the *Regulations* will expire on August 24, 2017.

2. Claims Construction

[159] Claim construction is a question of law to be determined by the Court. Where the meaning of terms or elements of claims are not apparent from a reading of the claim itself or from reference to the specification, the experts may provide guidance on this matter. The claims are to be construed, as they would be read by a Skilled Person, at the relevant date, looking to the patent with a view to understand. Justice Kane in *Alcon Canada Inc v Apotex Inc*, 2014 FC 699 cited Justice Hughes with approval on the principles of claim construction:

> [121] Justice Hughes provided a useful summary of the relevant principles following a review of all the jurisprudence in *Pfizer Canada Inc v Pharmascience Inc*, 2013 FC 120, [2013] FCJ No 111:
>
> > [64] There have been many judicial instructions as to the construction of a claim. To summarize:
> >
> > • construction must be done before considering the issues of validity and infringement;
> >
> > • construction is done by the Court alone, as a matter of law;
> >
> > • the Court is to construe the claim through the eyes of the person skilled in the art to which the patent pertains;
> >
> > • the Court may obtain the assistance of experts to explain the meaning of particular words and

> phrases, and as to the state of the art as of the date the claim was published;
>
> • the Court should read the claim in the context of the patent as a whole, including the description and other claims;
>
> • the Court should avoid importing this or that gloss from the description;
>
> • the Court should not restrict the claim to specific examples in the patent;
>
> • the Court should endeavour to interpret the claim in a way that gives effect to the intention of the inventor;
>
> • the Court should endeavour to support a meritorious invention.

[160] That said, there is no substantial dispute between the parties as to what is covered by the relevant claims. For completeness I will set out the claims in issue and their construction as advanced by the parties as identified in the following agreed Claims Chart. Note that while more are outlined below, only Claims 1, 8, 9, 33, 43 and 44 are asserted by Pfizer; the others are included for context:

Claim No.	**Depends From**	**Claim Language**	**Pfizer's Position on Construction**	**Teva's Position on Construction**
1.	None	A compound which is O-desmethyl-venlafaxine succinate or a mixed salt thereof.	***Not in issue.*** *Covers ODV succinate, or alternatively, a mixed ODV succinate salt, in any form.*	(BLANK)
2.	Claim 1.	A compound according to claim 1 wherein	***Not in issue.*** *Covers ODV*	(BLANK)

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Teva's Position on Construction
		the ratio of O-desmethyl-venlafaxine to succinic acid is 1:1.	*mono succinate in any form.*	
4.	Claim 1.	A compound according to claim 1 which is a hydrate of O-desmethyl-venlafaxine succinate.	***Not in issue.*** *Covers any hydrated form (i.e., a form in which water is present in the crystal lattice) of ODV succinate.*	(BLANK)
5.	Claim 1.	A compound according to claim 1 which is O-desmethyl-venlafaxine succinate monohydrate.	***Not in issue.*** *Covers any monohydrated form of ODV succinate (i.e., wherein there is one molecule of water present in the crystal lattice for every molecule of ODV succinate).*	(BLANK)
6.	Claims 1, 2, 4 or 5.	A compound according to any one of claims 1, 2, 4 and 5 wherein the salt is crystalline.	***Not in issue.*** *Covers any crystalline form of ODV succinate (or a mixed salt thereof). As it depends on claim 5, covers any crystalline form of ODV succinate monohydrate.*	(blank)

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Teva's Position on Construction
8.	Claim 6, which in turns depend from claims 1, 2, 4 or 5.	A compound according to claim 6 which exhibits an X-ray powder diffraction pattern having characteristic peaks expressed in degrees 2Θ (± 0.2^0 2Θ) at 10.20, 14.91, 20.56, 22.136, 23, 71, 24.60, and 25.79.	Covers Form I ODV (mono) succinate monohydrate (*i.e.*, the crystalline form of ODV succinate, which exhibits the characteristic XRPD peaks of Figure 1.)	(BLANK)
9.	Claim 6, which in turns depend from claims 1, 2, 4 or 5.	A compound according to claim 6 having an endotherm at about 131^0C.	Covers Form I ODV (mono) succinate monohydrate (*i.e.*, the crystalline form of ODV succinate, which exhibits a characteristic endotherm at about 131^0C.	(BLANK)
33.	Any one of the claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one claims 1 to 20 for the treatment of depression.	As it depends on claim 8 or 9, use of Form I ODV succinate for the treatment of depression.	(BLANK)
43.	Any one of the claims 1 to 20.	Use of therapeutically effective amount of sustained	As it depends on claim 8 or 9, use of a sustained release oral	As it depends on claims 8 or 9, use of therapeutically effective amount

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Teva's Position on Construction
		release oral dosage form comprising O-desmethyl;-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 prepared in a dosage to induce a blood plasma level no more than 225 ng/ml to lower the incidence of nausea, vomiting, diarrhea, abdominal pain, headache, vaso-vagal malaise, or trismus resulting from the oral administration of O-desmethyl-venlafaxine succinate.	dosage form comprising Form I ODV succinate to induce an average blood plasma level of no more than 225ng/ml to lower the overall incidence of the specified side effects as compared to oral administration of ODV succinate not so formulated.	of sustained release oral dosage form comprising Form I ODV succinate to induce a blood plasma level of no more than 225 ng/ml to lower the incidence of the specified effects as compared to oral administration of ODV succinate not so formulated.
44.	None.	A sustained release formulation comprising O-desmethyl-venlafaxine succinate and a pharmaceutically acceptable carrier or excipient, wherein the sustained release formulation provides peak serum levels of up	A sustained release formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I ODV succinate) which provides average peak serum levels up to 225 ng/ml.	A sustained released formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I OCD succinate) which provides peak serum levels of up to 225 ng/ml.

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Teva's Position on Construction
		to 225ng/ml.		

3. Obviousness

A. Introductory comments and summary

[161] Pursuant to s 28.3 of the *Patent Act*, an invention must not be obvious to a Skilled Person:

Invention must be obvious **28.3** The subject-matter defined by a claim in an application for a patent in Canada must be subject-matter that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to (a) information disclosed more than one year before the filing date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and (b) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere. [Emphasis added.]	**Objet non évident** **28.3** L'objet que définit la revendication d'une demande de brevet ne doit pas, à la date de la revendication, être évident pour une personne versée dans l'art ou la science dont relève l'objet, eu égard à toute communication : a) qui a été faite, plus d'un an avant la date de dépôt de la demande, par le demandeur ou un tiers ayant obtenu de lui l'information à cet égard de façon directe ou autrement, de manière telle qu'elle est devenue accessible au public au Canada ou ailleurs; b) qui a été faite par toute autre personne avant la date de la revendication de manière telle qu'elle est devenue accessible au public au Canada ou ailleurs. [Soulignement ajouté.]

[162] One of the two central issues in this case is obviousness, and its ancillary doctrine, obvious to try. In my respectful view, and the parties agreed, once the appropriate legal tests are resolved, the determination of both obviousness and obvious to try resolve into factual determinations based on the evidence and the patent before the Court. I have concluded on this aspect of the case that viewed through the eyes of the Skilled Person, and on a balance of probabilities that the invention claimed in the 668 Patent, including the inventive concepts of Claims 8, 9, 33, 43 and 44, were not obvious and were not obvious to try.

[163] In my view, the new composition of matter being the crystalline Form I ODV succinate, was ‘worth a try’. In addition, there were ‘possibilities’ that the Skilled Person would find the invention claimed in the 668 Patent through difficult experimentation particularly in respect of crystallization and polymorph screening. However, mere possibilities are not enough, and it is established that being ‘worth a try’ is not the test for obvious to try.

[164] On the evidence, I have concluded that Pfizer has established on a balance of probabilities that Teva’s allegation of obviousness including obvious to try are not justified.

B. The obviousness inquiry

[165] The key decision in the law of obviousness is that of the Supreme Court of Canada in *Apotex Inc v Sanofi Synthelabo Inc*, 2008 SCC 61 [*Sanofi* or *Plavix*] *Sanofi*.

[166] For convenience of reference and because of its centrality on this issue, I will set out *Sanofi* in its entirety both in terms of the legal test and its application to the facts, per Rothstein J. for the unanimous Court:

> (d) *Approach to Obviousness in Canada*
>
> …
>
> [64] While I do not think the list is exhaustive, the factors set forth by Kitchin J. and adopted by Lord Hoffmann in *Lundbeck*, referred to at para. 59 of these reasons, are useful guides in deciding whether a particular step was "obvious to try." However, the "obvious to try" test must be approached cautiously. It is only one factor to assist in the obviousness inquiry. It is not a panacea for alleged infringers. The patent system is intended to provide an economic encouragement for research and development. It is well known that this is particularly important in the field of pharmaceuticals and biotechnology.
>
> [65] In *Saint-Gobain PAM SA v. Fusion Provida Ltd.*, [2005] EWCA Civ 177 (BAILII), Jacob L.J. stated, at para. 35:
>
> > Mere possible inclusion of something within a research programme on the basis you will find out more and something might turn up is not enough. If it were otherwise there would be few inventions that were patentable. The only research which would be worthwhile (because of the prospect of protection) would be into areas totally devoid of prospect. The "obvious to try" test really only works where it is more-or-less self-evident that what is being tested ought to work.
>
> In *General Tire*, Sachs L.J. said, at p. 497:
>
> > "Obvious" is, after all, a much-used word and it does not seem to us that there is any need to go beyond the primary dictionary meaning of "very plain."
>
> In *Intellectual Property Law*, at p. 136, Professor Vaver also equates "obvious" to "very plain." I am of the opinion that the "obvious to try" test will work only where it is very plain or, to use the words of Jacob L.J., more or less self-evident that what is being tested ought to work.

[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.

[67] It will be useful in an obviousness inquiry to follow the four-step approach first outlined by Oliver L.J. in *Windsurfing International Inc. v. Tabur Marine (Great Britain) Ltd.*, [1985] R.P.C. 59 (C.A.). This approach should bring better structure to the obviousness inquiry and more objectivity and clarity to the analysis. The Windsurfing approach was recently updated by Jacob L.J. in *Pozzoli SPA v. BDMO SA*, [2007] F.S.R. 37 (p. 872), [2007] EWCA Civ 588, at para. 23:

> In the result I would restate the Windsurfing questions thus:
>
> > (1) (a) Identify the notional "person skilled in the art";
> >
> > (b) Identify the relevant common general knowledge of that person;
> >
> > (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
> >
> > (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
> >
> > (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention? [Emphasis added in original]

It will be at the fourth step of the *Windsurfing/Pozzoli* approach to obviousness that the issue of "obvious to try" will arise.

i. When Is the "Obvious to Try" Test Appropriate?

[68] In areas of endeavour where advances are often won by experimentation, an "obvious to try" test might be appropriate. In such areas, there may be numerous interrelated variables with which to experiment. For example, some inventions in the

pharmaceutical industry might warrant an "obvious to try" test since there may be many chemically similar structures that can elicit different biological responses and offer the potential for significant therapeutic advances.

ii. "Obvious to Try" Considerations

[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.

[71] For example, if the inventor and his or her team reached the invention quickly, easily, directly and relatively inexpensively, in light of the prior art and common general knowledge, that may be evidence supporting a finding of obviousness, unless the level at which they worked and their knowledge base was above what should be attributed to the skilled person. Their course of conduct would suggest that a skilled person, using his/her common general knowledge and the prior art, would have acted similarly and come up with the same result. On the other hand, if 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, including what turned out to be fruitless "wild goose chases", that evidence may support a finding

of non-obviousness. It would suggest that the skilled person, using his/her common general knowledge and the prior art, would have done no better. Indeed, where those involved including the inventor and his or her team were highly skilled in the particular technology involved, the evidence may suggest that the skilled person would have done a lot worse and would not likely have managed to find the invention. It would not have been obvious to him/her to try the course that led to the invention.

(e) Application to the Facts of This Case

[72] Applying the four steps of *Windsurfing/Pozzoli*, I accept the applications judge's findings of fact where they are unaffected by his rejection of the "obvious to try" test. Where application of the obvious to try test requires further consideration of the evidence, it will be necessary for this Court to make some findings of fact. In this case, I think it is preferable to remitting the matter to the trial judge for redetermination and subjecting his decision to further possible appeals.

[73] Apotex filed its notice of allegation in 2002. It is now some six years later. If the '777 patent is invalid, and provided all other requirements are met, Apotex should be entitled to a notice of compliance from the Minister without any further delay. Indeed, the *NOC Regulations* are intended to be a summary procedure. I think it is time that this matter finally be resolved. I would conduct the following analysis:

i. Identify the Notional Person Skilled in the Art

[74] Both parties agreed that a trained pharmachemist is that person.

ii. Identify the Relevant Common General Knowledge of That Person

[75] Apotex reiterates its submissions made with respect to anticipation, insisting that, since the methods of separation were well known, the claimed invention and its advantages would have been obvious to the person skilled in the art. Shore J. found on the evidence before him that there were five well-known methods to separate this racemate into its isomers. However, he did not find that the relative advantage of the dextro-rotatory isomer would have been known by the skilled person.

iii. Identify the Inventive Concept of the Claim in Question or, if That Cannot Readily Be Done, Construe It

[76] The construction of the claims in the ‘777 patent is not an issue. It is agreed that they constitute the dextro-rotatory isomer of the racemate and its pharmaceutically acceptable salts and processes for obtaining them.

[77] The inventive concept of the claims is not readily discernable from the claims themselves. A bare chemical formula in a patent claim may not be sufficient to determine its inventiveness. In such cases, I think it must be acceptable to read the specification in the patent to determine the inventive concept of the claims. Of course, it is not permissible to read the specification in order to construe the claims more narrowly or widely than the text will allow.

[78] In the present case, it is apparent that the inventive concept of the claims in the ‘777 patent is a compound useful in inhibiting platelet aggregation which has greater therapeutic effect and less toxicity than the other compounds of the ‘875 patent and the methods for obtaining that compound.

iv. Identify What if Any Differences Exist Between the ‘875 Patent and the ‘777 Patent

[79] The ‘875 patent disclosed over 250,000 possible different compounds predicted to inhibit platelet aggregation. Twenty-one compounds were made and tested. Nothing distinguishes the racemate in this case from other compounds disclosed or tested in terms of therapeutic effect or toxicity. As stated above, there is no disclosure in the ‘875 patent of the specific beneficial properties associated with the dextro rotatory isomer of this racemate in isolation; nor was there disclosure of any advantages which flow from using the bisulfate salt of the dextro rotatory isomer. The ‘875 patent did not differentiate between the properties of the racemate, its dextro-rotatory isomer and levo-rotatory isomer or indeed the other compounds made and tested or predicted to work.

[80] On the other hand, the ‘777 patent claims that the invention of the dextro rotatory isomer of the racemate, clopidogrel, and its bisulfate salt discloses their beneficial properties over the levo rotatory isomer and the racemate and expressly describes how to separate the racemate into its isomers.

v. Viewed Without Any Knowledge of the ‘777 Patent, Do Those Differences Constitute Steps Which Would Have Been Obvious to the Person Skilled in the Art or Do They Require a Degree of Inventiveness?

[81] At this stage, it must be determined whether the nature of the invention in this case is such as to warrant an "obvious to try" test. The discovery of the dextro-rotary isomer and its bisulfate salt came after experimentation. There were interrelated variables with which Mr. Badorc had to experiment. An "obvious to try" test in this case would recognize the evidence of the expert witnesses as to the discovery of the beneficial properties of the dextro-rotary isomer and its bisulfate salt and the methods for finding them.

[82] The applications judge cannot be faulted for the analysis he conducted as far as it went. However, he erred in not allowing for the application of the "obvious to try" test, which is warranted in this case.

[83] The following factors are therefore relevant at this fourth step of the obviousness inquiry:

(1) *Is It More or Less Self-Evident That What Is Being Tried Ought to Work?*

[84] As I have observed earlier, Shore J. found that the skilled person would not know, before separating this particular racemate into its isomers and then testing the separated isomers, that the properties of the dextro rotatory isomer would be different from the properties of the racemate or the levo rotatory isomer (para. 81). Similarly, he found that the person skilled in the art would not know before trying the different salts in combination with the dextro rotatory isomer what the bisulfate salt's beneficial properties would be (para. 82).

[85] Just because there are known methods of separating a racemate into its isomers does not mean that a person skilled in the art would necessarily apply them. The fact that there are such known methods of separation will be of no account if the evidence does not prove that it was more or less self-evident to try them. It is true that at the relevant time there was evidence that a skilled person would know that the properties of a racemate and its isomers might be different. However, a possibility of finding the invention is not enough. The invention must be self-evident from the prior art and common general knowledge in order to satisfy the "obvious to try" test. That is not the evidence in this case.

(2) *What Is the Extent, Nature and Amount of Effort Required to Achieve the Invention?*

[86] As indicated, the applications judge found that there were five well-known techniques for separating this racemate into its

isomers. He also found that there was no evidence that at the relevant time, a person skilled in the art would know which one would work with the racemate at issue in this case. The evidence was that a skilled person would eventually find the right technique.

[87] As earlier indicated, Shore J. also found that there was no evidence that at the relevant time a person skilled in the art would know before separating the racemate and testing the isomers what their properties would be, although the specific properties of the isomers could be discovered. There was evidence that, using known techniques, the properties of different pharmaceutically acceptable salts to be used with the dextro-rotatory isomer could be discovered.

[88] However, in considering whether it was "obvious to try" to find the invention, once it was decided to isolate the dextro-rotatory isomer, the methods for doing so were known, the methods for testing the properties of the isomers were known and the method for determining the beneficial properties of the salts to be used with the isomer would also have been known.

[89] According to Mr. Badorc's affidavit, it took from November 1985 to April 1986 to find the '777 invention, and he was already familiar with the '875 invention. Potentially five different methods to separate the racemate would have had to have been tried and tested before determining the properties of the dextro-rotatory isomer. As in the case of anticipation, one might infer that the applications judge, if asked to decide this question, would have held that the investigation here was not routine, but rather was prolonged and arduous. In any event, on the facts of this case, this factor would assume small significance in view of the finding I make with respect to the whole course of conduct discussed at para. 91 below.

(3) *Is There a Motive From the Prior Art to Find the Solution That the '777 Patent Addresses?*

[90] It is well known that the pharmaceutical industry is intensely competitive. Market participants are continuously in search of new and improved medications and want to reach the market with them as soon as possible. So demand for an effective and non-toxic product to inhibit platelet aggregation might be assumed to exist. However, nothing in the '875 patent or common general knowledge provided a specific motivation for the skilled person to pursue the '777 invention. The prior patent was a genus patent, and selection might be expected. However, the prior patent did not differentiate between the efficacy and the toxicity of any of

the compounds it covered. This suggests that what to select or omit was not then self-evident to the person skilled in the art.

(4) *What Is the Course of Conduct Which Was Followed Which Culminated in the Making of the Invention?*

[91] Mr. Badorc's affidavit reveals that for several years prior to November 1985, Sanofi was in the process of developing the racemate in its salified form. In November 1985, the racemate was being tested in preliminary human clinical trials. It was at that time that Mr. Badorc was asked to separate the racemate into its isomers. After he discovered that the dextro-rotatory isomer was active and non-toxic and that the levo-rotatory isomer was non-active and toxic, Sanofi decided to develop the dextro-rotatory isomer and abandon its work on the racemate. However, this was after it had "spent millions of dollars and several years developing [the racemate] up to the point of preliminary human clinical trials" without at least trying to see if the dextro rotatory isomer had advantageous properties to those of the racemate (Affidavit of Mr. Badorc, at para. 25). This evidence was uncontradicted.

(5) *Was the Invention of the '777 Patent "Obvious to Try"?*

[92] The methods to obtain the invention of the '777 patent were common general knowledge. It can be assumed that there was a motive to find a non-toxic efficacious product to inhibit platelet aggregation in the blood. However, it was not self-evident from the '875 patent or common general knowledge what the properties of the dextro-rotatory isomer of this racemate would be or what the bisulfate salt's beneficial properties would be and therefore that what was being tried ought to work. The course of conduct and the time involved throughout demonstrate that the advantage of the dextro-rotatory isomer was not quickly or easily predictable. Had the dextro-rotatory isomer been "obvious to try", it is difficult to believe that Sanofi would not have opted for it before unnecessary time and investment were spent on the racemate. I conclude that the prior art and common general knowledge of persons skilled in the art at the relevant time were not sufficient for it to be more or less self-evident to try to find the dextro-rotatory isomer.

> (f) *Conclusion on Obviousness*
>
> [93] As I have earlier explained, there was a significant difference between the ‘875 genus patent and the ‘777 selection patent. The difference was not obvious. Having regard to the foregoing analysis, I conclude that the allegation of obviousness is not justified.
>
> [Emphasis added except where in original.]

[167] The Supreme Court in *Sanofi* made new patent law for Canada; the Supreme Court held there may be circumstances where an obvious to try analysis could be conducted - previously, obvious to try was not allowed as a test of obviousness.

[168] I note that the Supreme Court in *Sanofi* provided guidance concerning obvious to try at the outset of its analysis:

> [64] However, the “obvious to try” test must be approached cautiously. It is only one factor to assist in the obviousness inquiry. It is not a panacea for alleged infringers. The patent system is intended to provide an economic encouragement for research and development. It is well known that this is particularly important in the field of pharmaceuticals and biotechnology.
>
> [65] Mere possible inclusion of something within a research programme on the basis you will find out more and something might turn up is not enough. If it were otherwise there would be few inventions that were patentable. The only research which would be worthwhile (because of the prospect of protection) would be into areas totally devoid of prospect. The “obvious to try” test really only works where it is more-or-less self-evident that what is being tested ought to work.
>
> …
>
> I am of the opinion that the “obvious to try” test will work only where it is very plain or, to use the words of Jacob L.J., more or less self-evident that what is being tested ought to work.

> [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.

[169] According to this guidance, obvious to try "must be approached cautiously." The obvious to try test "is only one factor to assist in the obviousness inquiry." The Supreme Court added that obvious to try "is not a panacea for alleged infringers." The Supreme Court added relevant context to these principles in para 64: "[T]he patent system is intended to provide an economic encouragement for research and development. It is well known that this is particularly important in the field of pharmaceuticals and biotechnology."

[170] In the next paragraph, para 65, the Supreme Court confirmed that: "[M]ere possible inclusion of something within a research programme on the basis you will find out more and something might turn up is not enough. If it were otherwise there would be few inventions that were patentable. The only research which would be worthwhile (because of the prospect of protection) would be into areas totally devoid of prospect. The 'obvious to try' test really only works where it is more-or-less self-evident that what is being tested ought to work."

[171] It recapped these parameters in para 66 stating:

> [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.

C. Federal Court of Appeal Jurisprudence

[172] The Federal Court of Appeal has addressed the obvious to try analysis in several cases decided after *Sanofi*.

[173] In *Pfizer v Apotex*, 2009 FCA 8, the Federal Court of Appeal per Noël J.A. rejected the proposition, advanced on the basis of English law, that if the prior art indicates that "something may work", and the motivation is such as to make this avenue "worthwhile" to pursue, the obvious to try test is satisfied:

> [45] In contrast, the test applied by Mr. Justice Laddie appears to be met if the prior art indicates that something may work, and the motivation is such as to make this avenue "worthwhile" to pursue (Pfizer Ltd., supra, para. 107, as quoted at para. 42 above). As such, a solution may be "worthwhile" to pursue even though it is not "obvious to try" or in the words of Rothstein J. even though it is not "more or less self-evident" (Sanofi-Synthelabo, supra, para. 66). In my view, this approach which is based on the possibility that something might work, was expressly rejected by the Supreme Court in Sanofi-Synthelabo, at paragraph 66.
>
> [Emphasis added.]

[174] In *Novartis*, after referring to *Sanofi*, Justice Hughes discusses the Federal Court of Appeal's decision in *Sanofi-Aventis v Apotex Inc*, 2013 FCA 186 [*Plavix 2*]:

> [64] These principles have been applied recently by the Federal Court of Appeal in *Sanofi-Aventis v Apotex Inc*, 2013 FCA 186, wherein the Court of Appeal found that the Trial Judge had erred in concluding that if the necessary techniques were available to arrive at the alleged invention, the invention itself was obvious. Pelletier JA (with whom Noël JA agreed) wrote at paragraphs 73 and 74:
>
> > *73 With these facts in mind, the Supreme Court articulated why the separation of the racemate was*

not obvious to try. It held that just because the methods of separating a racemate into its isomers are known, it does not follow that a person skilled in the art would necessarily apply them. The Supreme Court explained:

> *It is true that at the relevant time there was evidence that a skilled person would know that the properties of a racemate and its isomers might be different. However, a possibility of finding the invention is not enough. The invention must be self-evident from the prior art and common general knowledge in order to satisfy the "obvious to try" test. That is not the evidence in this case.*
>
> *Plavix, cited above, at paragraph 85*
>
> *However, the prior patent did not differentiate between the efficacy and the toxicity of any of the compounds it covered. This suggests that what to select or omit was not then self-evident to the person skilled in the art.*
>
> *Plavix, cited above, at paragraph 90*

74 What emerges from this review of the Supreme Court's decision in Plavix, cited above, is that the key factor in its "obvious to try" analysis was the lack of knowledge of the properties of the enantiomers of the compounds of the '875 Patent, including the racemate from which clopidogrel was obtained. Absent that knowledge, it was not obvious to try to resolve the racemate, or any other compound, so as to obtain the enantiomer having those advantageous properties.

and at para 81:

81 Given that the Trial Judge applied the test for obviousness set out in Plavix, and given that he applied it to the same material facts as the Supreme Court, he ought to have come to the same conclusion. His error lay in failing to recognize that the unknown nature of the properties of the enantiomers of PCR 4099, or of any of the other compounds of the '875 Patent, was fatal to the

> *"obvious to try" analysis. Put another way, the distance between the common general knowledge and the inventive concept of the '777 Patent could not be bridged by routine experimentation since the results to be obtained were unknown. On the facts, this was confirmed by the fact that the inventors, who had more knowledge that the person of ordinary skill in the art, attempted to resolve a number of other compounds before finally trying PCR 4099: see Reasons, at paragraphs 752-759.*

[65] Gauthier JA wrote concurring reasons. At para 137 she wrote:

> *137 The Trial Judge believed that the evidence before him with respect to the separation of the enantiomers was significantly different from the evidence before the Supreme Court of Canada in Plavix because: i) he found that a line had been drawn in the sand at the time the application was filed, and that as part of the process of developing a racemic drug a sponsor would be motivated to separate the enantiomers to get information to pre-empt expected new regulatory requirements (See Reasons at paragraphs 748-749); and ii) in his view, the separation itself did not involve substantial difficulties and was routine. However, Rothstein J. made it clear in Plavix that whether the separation or resolution of the enantiomers was routine or involved arduous work would assume small significance in this case when one considers the whole course of conduct that led to the decision to separate (See Plavix at paragraph 89).*

[175] In *Eli Lilly v Mylan*, 2015 FCA 286, per Dawson J.A., the Federal Court of Appeal at para 4, declined to agree with the application of an obvious to try test defined as "whether the skilled person had good reason to pursue predictable solutions or solutions that provide a 'fair expectation of success'." Instead, the Court of Appeal stated: "…. that the correct test, and the test that ought to be applied by the Federal Court, is that articulated by the Supreme Court of Canada in *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61, [2008] 3 SCR 265, at

para 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.”

[176] Shortly after the hearing in the case at bar, the Federal Court of Appeal released *Bristol-Myers Squibb Canada Co et al v Teva Canada Limited*, 2017 FCA 76 [*Atazanavir*]. I therefore invited the parties to make written submissions on *Atazanavir*.

[177] In *Atazanavir*, per Pelletier J.A., the Federal Court of Appeal considered the obviousness inquiry and the doctrine of obvious to try. The Court of Appeal confirmed that the innovative feature of the Supreme Court’s decision in *Sanofi* in relation to obviousness was its adoption of the “obvious to try” test [para 34].

[178] At para 38 the Court said that “… the Supreme Court was quick to add that ‘the ‘obvious to try’ test must be approached cautiously” because it “is only one factor to assist in the obviousness inquiry”: *Plavix 1* at para 64.

[179] The Federal Court of Appeal confirmed that:

> [60] The reasonable conclusion to be drawn from these expressions of caution is that the ‘obvious to try’ test has not displaced all other inquiries into obviousness. Indeed, that is what this Court concluded in *Wenzel Downhole Tools Ltd v National-Oilwell Canada Ltd*, 2012 FCA 333, [2014] 2 FCR 459 at para 105.

[180] In this connection the Federal Court of Appeal in *Atanazavir* also referred to the test for obviousness prior to *Sanofi* which test had been set out by the Federal Court of Appeal in *Beloit Canada Ltd v Valmet OY* (1986), 64 NR 287, 8 CPR (3d) 289 at 294 (FCA) [*Beloit*]:

> [61] While the Supreme Court accepted the 'obvious to try' test as a way of addressing the issue of obviousness, other inquiries remain possible, including the *Beloit* test, subject to the Court's warnings about a rigid 'acontextual' application of that test, or of any other for that matter.

[181] The *Beloit* test referred in *Atanazavir* set out the previous established obviousness test:

> The classical touchstone for obviousness is the technician skilled in the art but having no scintilla of inventiveness or imagination; a paragon of deduction and dexterity, wholly devoid of intuition; a triumph of the left hemisphere over the right. The question to be asked is whether this mythical creature (the man in the Clapham omnibus of patent law) would, in the light of the state of the art and of common general knowledge as at the claimed date of invention, have come directly and without difficulty to the solution taught by the patent.

[182] The Federal Court of Appeal held that *Sanofi* did not the change the definition of obviousness:

> [65] It may be helpful to keep in mind that the obviousness analysis asks whether the distance between two points in the development of the art can be bridged by the Skilled Person using only the common general knowledge available to such a person. If so, it is obvious. The first of those points is the state of the prior art at the relevant date. References in the jurisprudence to "the inventive concept", "the solution taught by the patent", "what is claimed" or simply "the invention" are attempts to define the second point.
>
> [66] Prior to *Plavix 1*, the jurisprudence followed *Beloit* and treated the second point as "the solution taught by the patent" which was often treated as synonymous with "what is claimed in the patent" or "the invention": *Proctor & Gamble Pharmaceuticals Canada Inc. v. Canada (Minister of Health)*, 2004 FCA 393,

> [2005] 2 F.C.R. 269 at para. 47, *Pfizer Canada Inc. v. Canada (Health)*, 2007 FCA 209, 366 N.R. 347 at para. 133, *Novopharm Limited v. Janssen-Ortho Inc.*, 2007 FCA 217, 366 N.R. 290 at para. 25. The question is whether the "inventive concept" was intended to redefine the second point as it was understood to be prior to *Plavix 1*. I note that in the passage from *Pozzoli* quoted above, the English Court of Appeal did not consider the "inventive concept" to have changed anything of substance. If the parties could not agree on it, it could be forgotten. It went on to say at paragraph 19 of its reasons: "In the end what matters is/are the difference(s) between what is claimed and the prior art." This is essentially the state of Canadian law prior to *Plavix 1*.
>
> [67] Is it the case that changing one of the two points I referred to earlier amounts to changing the definition of obviousness? Given that obviousness is concerned with whether bridging the difference between the prior art and a second point requires inventiveness, changing the second point will affect the difficulty of bridging that difference, therefore making inventiveness more or less likely. If that is so, is it reasonable to conclude that the Supreme Court intended to change the definition of the obviousness analysis when it adopted, without commentary, the *Windsurfing/Pozzoli* framework? Is it likely that the Supreme Court, having taken great care in modifying the test for obviousness, would, without saying so, change the definition of obviousness?
>
> [68] My inclination is to believe that the Supreme Court does not change substantive law by implication, particularly when it has shown a cautious approach to change in the same context: see *Apotex Inc. v. Eli Lilly Canada Inc.*, 2016 FCA 267, 142 C.P.R. (4th) 171 at para. 37.
>
> [Emphasis added.]

[183] In *Atanazavir* the Federal Court of Appeal clarified the definition of "inventive concept" (and see in this respect para 65 just quoted above):

> [75] For the reasons set out above, I find that the "inventive concept" is not materially different from "the solution taught by the patent." Had the Federal Court applied that definition to the facts, it would have found that the inventive concept in this case is atazanavir bisulfate, a salt of atazanavir which is pharmaceutically acceptable because it has equal or better bioavailability than the

> atazanavir free base. Atazanavir's limited bioavailability was the source of the motivation to pursue the solution. The fact that claim 2 of the '736 patent claims a pharmaceutical dosage form of Type-I atazanavir bisulfate confirms its acceptability for pharmaceutical purposes.

D. Analysis of Obviousness

[184] With these principles in mind, I proceed with the analysis of obviousness as set out by the Supreme Court in *Sanofi*.

E. Identify the notional "person skilled in the art"

[185] A patent is addressed to the person of ordinary skill in the art [Skilled Person], who is defined in the jurisprudence as being "unimaginative and uninventive, but at the same time is understood to have an ordinary level of competence and knowledge incidental to the field to which the patent relates and to be reasonably diligent in keeping up with advances": *AstraZeneca Canada Inc v Apotex Inc*, 2014 FC 638 at para 51 (citing *Merck & Co v Pharmascience Inc*, 2010 FC 510 at paras 34-40), aff'd 2015 FCA 158. In *Beloit*, the Federal Court of Appeal refers to the Skilled Person as an "unimaginative skilled technician", and see *AstraZeneca Canada Inc v Apotex Inc*, 2014 FC 638 at para 51 (Rennie, J as he then was) (citing *Merck & Co v Pharmascience Inc*, 2010 FC 510 at paras 34-40 (Hughes, J)), aff'd 2015 FCA 158 (per Dawson, J.A.).

[186] In this case, the parties agree that the Skilled Person would be a person or team of people who would have at least a bachelor's degree in chemistry, pharmaceutics or a related field, and

relevant practical experience in fields such as pharmaceutical chemistry or pre-clinical drug development or pharmacokinetics.

[187] The parties disagree on whether the Skilled Person in addition requires clinical or medical expertise: Teva says the Skilled Person requires clinical or medical expertise, which Pfizer disputes. On cross-examination, Dr. Lieberman (a clinical psychiatrist and expert tendered by Teva) acknowledged that clinical experience was not required to read and understand the 668 Patent, including the information about clinical trials and side effects. Teva's expert also agreed that a skilled person could expect that a change in formulation could address tolerability related side effects or tolerability kinds of side effects. Dr. Lieberman also agreed that someone who is a formulator or a pharmacologist, for example could understand that by preparing a sustained release formulation, they might be able to reduce certain GI related and other side effects. I note in this connection that the 668 Patent does not specify any particular dosage in Claim 43 which instead speaks of "use of a therapeutically acceptable amount"; the 668 Patent does not make a claim on a 75 mg or 50 mg or 100 mg or any particular amount of the drug. I take this to mean that the "therapeutically acceptable amount" of the medicine claimed is to be determined by a person with medical expertise dealing with his or her patient. In these circumstances, and in my respectful view, the Skilled Person does not require clinical or medical expertise.

F. Identify the relevant common general knowledge of the Skilled Person

[188] The parties disagree as to what constitutes the common general knowledge of the Skilled Person.

[189] There was some agreement on the common general knowledge and state of the art at February 12, 2001. The parties agree that general methods and techniques for salt and crystal formation and preparation of sustained release dosage forms were known in the art. Additionally, the person of ordinary skill would know that ODV had been disclosed and claimed as an active metabolite of venlafaxine and as a member of a class of compounds in several patents: ODV was disclosed in US186, CA 540 and WO 851.

[190] It is also agreed that the prior art disclosed ODV both as a free base and a fumarate salt, and that other pharmaceutically acceptable salts (including succinate, among at least eleven (11) others as set out in US 186 at column 2, ll. 35 et seq.; the same eleven were identified in CA 540; WO 851 listed twenty-six other pharmaceutically acceptable non-toxic acids that might be reacted to form salts of ODV.

[191] 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 either ODV succinate or Form I ODV succinate.

[192] 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 81 of his affidavit, and in the nature of a research program, not routine experimentation. Even though a Skilled Person may have had some general expectations about which salts may form, these expectations were theoretical and the common 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 Skilled Person would know 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."

[193] The Skilled Person also knew that even successfully forming a salt was but one part of the puzzle; he or she knew that to prepare pharmaceutical salts for formulation into pharmaceutical drugs, they were typically looking for a stable crystalline solid. However, whether or not a particular salt formation experiment would result in crystals - to say nothing of stable crystals - was not known or predictable. Skilled persons would not know in advance how a crystalline solid (if any) of a given compound could be made, how many different crystal forms of that compound might exist (including hydrated and solvated forms), what those forms would be, or what properties those forms would have. They would know that some salts might crystallize, some might form amorphous forms, but they would also know that other salts would neither form into crystals.

[194] The Skilled Person would know generally of the existence of crystalline and polymorph screening. As Dr. Park deposed (see para 129 and following above), polymorph screening was not rote work, was difficult and in her experience which was considerable, required skill and judgment. It was not possible to predict at the outset of a polymorph screen how many solid forms would identified, what they would be, or what solid forms would result from any particular method or set of conditions. Therefore, as Dr. Park deposed from her experience, and Dr. Myerson deposed as an expert on the subject, this process often required numerous experiments and analyses, and strategy and judgment has to be employed to make decisions about how to proceed based on the results that we obtained such that the number of potential experiments that can be conducted is extremely large.

[195] I accept what Dr. Myerson deposed in connection with both the matter of salt screens and the matter of crystalline and polymorph screening. Dr. Myerson was a professor of Industrial Pharmacy and Pharmaceutics at MIT; in my view his evidence was comprehensive and credible. He has what I consider to be very considerable research and academic experience in industrial crystallization and the crystallization of pharmaceutical solids - the matters at hand in relation to Form I ODV succinate. His evidence in connection with the crystal and polymorph screening process is corroborated by the experience of Dr. Park, which I have accepted at paras 129 and following of these Reasons. I appreciate that Dr. Park is a named inventor on the 668 Patent, but this did not detract from her evidence.

[196] Dr. Myerson deposed:

Choosing an Appropriate Salt

54. In order to determine if a compound can form salts and if so to find the most appropriate salts of a given active compound for development, scientists will attempt to make and test a number of different salts and examine their properties in a process called a "salt screen." If the active compound is a base, a salt screen will be directed at finding an acid that is potentially capable of forming a salt with that free base. Conversely, if the active compound is acidic, the salt screen involves finding a base that is capable of forming a salt with the free acid.

55. During a salt screen experiment for a free base, scientists will dissolve the free base and a potential acidic salt former in solution and attempt to precipitate a salt from the mixture by changing the conditions of the system. These experiments involve using different conditions of concentration and temperature, and different solvents and solvent mixtures. The experiments would be repeated for each potential counterion (*i.e.*, acid).

56. The main purpose of the salt screen is to determine whether salts of the compound can be prepared with the different counter-ions under consideration, whether the salt formed is crystalline, and whether the form is stable. The choice of potential acids (or bases) for pharmaceutical salt formation can be large. It is not limited to those counterions that had been previously used in approved pharmaceutical products, but would include any acid present in food or drink that are generally regarded as safe.

57. <u>The salt selection and formation process is highly unpredictable. Indeed, one cannot predict prior to actually attempting to form a salt whether the reaction of a given active drug compound with a particular acid or base will successfully produce a salt or what the properties of that salt will be.</u>

58. Once a salt form is found with a particular counterion, that salt is then typically subjected to a solid form (polymorph) screen, which consists of another set of experiments conducted over a variety of different conditions to determine what, if any, crystalline forms exist for that particular salt.

59. The solid form of a particular salt form can significantly influence a number of physical and chemical properties of the API including solubility, dissolution rate, chemical stability, hygroscopicity, crystal shape and manufacturing/processing

characteristics. Scientists cannot predict how the formation of a particular solid form of a salt will affect these properties prior to successful formation and analysis of the salt and its solid forms. Therefore, it is not possible to predict in advance of actually making the salt whether its formation will yield any solid form (crystalline or amorphous), much less one with more desirable properties than those of the free base or other salt forms of the drug.

Crystalline and Amorphous Solids

60. Crystals are solids in which the constituent atoms or molecules are arranged in a periodic repeating pattern that extends in three dimensions. When crystals are grown slowly and carefully they are normally bounded by plane faces (flat surfaces extending in different directions) that can be seen with the naked eye. Looking at a common material such as table salt under a magnifying glass will reveal these plane faces. They can also be seen in the beautiful mineral samples that are often displayed in museums.

61. Not all crystalline materials display these obvious plane faces. Materials such as steel, concrete, bone, and teeth are made up of small crystals that can be seen under a light or electron microscope. Still other materials, such as wood, silk, hair, and many solid polymers (plastics) are only partially crystalline or have crystalline regions.

62. Solids that are not crystalline and have no long range order – for example, glass – are said to be amorphous. Amorphous solids are often (but not always) less chemically stable than crystalline solids (an undesirable property for pharmaceuticals). However, they are typically more soluble than crystalline materials (a desirable property for pharmaceuticals). There are a number of reasons why a compound might form as an amorphous solid, rather than a crystalline solid. One common reason is the presence of impurities that block the formation of the crystalline lattice (explained below). Materials can also be mixtures of crystalline and amorphous solids. For example, a sample can be largely amorphous with some crystalline content and vice versa.

63. Crystals are made up of molecules that interact with each other to form chemical bonds of different kinds. They are usually classified as ionic, covalent, metallic, van der Waals, or hydrogen bonds, with the first three types being stronger than the last two. Organic molecules (molecules containing carbon) form crystals which are known as molecular crystals, in which the molecules are

held together in the crystal form by weak attractive van der Waals forces.

64. The internal structure of a molecular crystal, called the crystal structure or crystalline lattice, is determined by the position of the molecules relative to each other in a three dimensional space. Different salts of the same parent compound will have different crystal structures, because they will be comprised of different molecules.

65. The process by which crystals are formed is called crystallization. Crystallization from solution is the most common crystallization method. In this method, crystallization is induced by changing the state of the system to reduce the solubility of the substance of interest. The change of state can be brought about by cooling, evaporation of solvent, changing of solvent composition, chemical reaction, or pH change. This change of state results in formation of a crystalline solid through processes known as nucleation (the birth of new crystals) and crystal growth (the growth of the nuclei to larger sizes).

66. Nucleation of the initial crystal is unpredictable, and it is often difficult to crystallize a newly synthesized compound for the first time. Once the initial crystal is obtained, it can be used to "seed" solutions to assist in further crystallization 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.

Polymorphism

67. Some chemical species can crystallize into more than one three-dimensional crystal structure. This phenomenon is called polymorphism (or allotropism if the species is an element, such as carbon). While polymorphism is relatively common among organic molecules, whether or not a particular compound is capable of polymorphism – and if so how many different polymorphs may exist – cannot be predicted and must be determined empirically (to the extent possible to do so).

68. Different polymorphs of the same material can display very different properties. A dramatic example is carbon, which can crystallize as graphite or as diamond. Properties such as hardness, density, electrical conductivity and shape are very different for these two solids although they are both crystalline. These significant differences in properties, brought about by differences

in crystal structure, are not unique to carbon; they can occur in all materials that display polymorphism. Other properties that normally vary among polymorphs of a given substance include solubility, dissolution rate, and vapor pressure, among others.

69. At a particular temperature, one polymorph will be the thermodynamically stable form (of the polymorphs currently known for a given compound). This does not mean that other polymorphs cannot exist under those conditions; it means only that one polymorph is stable and any others present can convert to the stable polymorphic form over time. The rate of this transition, or whether it occurs at all, is dependent on various conditions, such as temperature, pressure, presence of solvent, the relative stability of the crystal forms and the solubility of the polymorph(s).

…

Pseudo-polymorphism

71. The discussion above relating to the thermodynamic stability of polymorphs only applies to single component solid forms (true polymorphs). Another related category of solid forms are known as pseudo-polymorphs.

72. Pseudo-polymorphism refers to the ability of certain compounds to crystallize in a structure that contains a solvent as part of the crystal lattice. These crystals are also known as solvates. A solvate in which the solvent is water is usually referred to as a hydrate. For a given pseudo-polymorph, the ratio of the number of molecules of solvent to the number of molecules of the chemical species itself is usually fixed. This is referred to as its stoichiometry. These forms are referred to as pseudo-polymorphs because although they involve the same compounds, they also include solvent molecules as part of the structure.

73. Each pseudo-polymorph of a given stoichiometry itself can have polymorphs, so a compound can have polymorphs of the compound itself (single component) and if the compound for example, has a monohydrate and a dihydrate form, each of these forms can also have polymorphs.

74. Different crystal forms of an API will have different properties from each other and will also differ from the amorphous form. In addition, solvates and hydrates will also have different properties from other crystal forms and from each other. These differences in properties of solid forms can significantly impact the manufacturability, performance and/or quality of the drug product.

75. The thermodynamic stability of a compound therefore becomes more complicated when looking at systems which have multiple polymorphs and pseudo-polymorphs (and polymorphs of pseudo-polymorphs). Statements about stability must include both the temperature and the presence of solvent. For example, in discussing the relative stability of hydrates to a non-hydrated form (or of hydrates to each other) both the temperature and the presence of water must be specified.

76. Like the different polymorphs of a given compound, it is also not possible to predict in advance whether or not a compound may have one or more pseudo-polymorphs and if so, what those pseudo-polymorphs may be. Knowledge of the existence of polymorphs or pseudopolymorphs for one compound does not provide useful information about the existence of polymorphs or pseudopolymorphs of a different compound (even if the compounds are structurally similar, or are different salts of the same molecule).

…

Importance of Polymorphs in Pharmaceutical Industry

77. Changes in a compound's solid state form can result in significant differences in its chemical and physical characteristics. These differences can affect the manufacturability, performance and/or quality of the drug product. Since many important pharmaceutical compounds display polymorphism and pseudo-polymorphism (and can therefore exist in different forms), the study of a compound's crystal form is extremely important in the pharmaceutical industry.

78. One of the most well-known episodes demonstrating the importance of polymorphism in pharmaceuticals involves the antiretroviral drug ritonavir (Norvir). In 1998, after the drug had been approved and was on the market, a more stable, less soluble crystalline form appeared in the formulation that caused dissolution failures of the soft gelatin capsules. Because the new polymorph was less soluble, less of the drug was absorbed in the bloodstream, and the dosage form contained in the soft-gels no longer worked. The product was withdrawn from the market because the manufacturing process was no longer able to produce the desired polymorph reliably. The manufacturer later learned that the presence of a low-level impurity in the process had been inhibiting the formation of a more stable form. Once that impurity was no longer present, the more stable – and less soluble – form emerged. Eventually the product was reformulated with the more

stable polymorph and relaunched. This demonstrates that when evaluating polymorph stability, you can only indicate that a given form is the most stable form of those discovered to date, as it is always possible to potentially discover a new, more stable form.

79. In addition, the most stable form of a compound known is not necessarily the form that has the desired properties. The history of paracetamol (also known as acetaminophen) exemplifies the difficulties encountered in identifying the appropriate polymorph for pharmaceutical formulations. In the mid-1990s, Wyeth first attempted to use the thermodynamically stable Form I in pharmaceutical formulations. However, its crystal structure exhibited certain properties that made it extremely expensive and troublesome to make in an oral formulation. Other polymorphs were difficult to isolate and obtain in a stable form. One polymorph was observed only in fusion experiments, and was reported to be so unstable that no crystals had been isolated to date. The third polymorph, Form II, had been almost impossible to reproduce reliably for over 20 years. Wyeth spent a significant amount of resources to reliably crystallize Form II before realizing that Form II converted to Form I if allowed to remain in solution or stored without drying, but did not convert to Form I if it was ground or compressed. This further illustrates how variations in experimental and manufacturing conditions can mask the existence of other polymorphs, including those which may be better suited for pharmaceutical formulations than the most stable polymorph known for the compound.

80. Today, the search for crystalline forms, including polymorphs, solvates and hydrates, has become a significant part in the development of new pharmaceutical products. Polymorph screening is time consuming with no ability to predict success in identifying a suitable solid-state form for development. Solid form screening for a given compound can involve thousands of experiments performed over many months or even longer. There is no “standard” method for performing a solid form screen and the number of experiments and conditions that are tried are dependent on the choices made by the investigator and the time allotted to the screen.

81. While the general methods to perform crystallizations at different conditions and with different solvents were known in the art as of the early 2000s, there are a wide variety of combinations of variables such as, solvents, solvent mixtures, temperatures, cooling rates, evaporation rates, etc. that could be used to attempt to generate new solid state forms. Thus, the number of potential experiments that can be conducted is extremely large.

82. Overall, given a particular compound, a person skilled in the art in the early 2000s would not be able to predict:

> (a) whether he or she would be able to make any crystal form of that compound;
>
> (b) if so, what level of effort would be required to obtain it;
>
> (c) what its properties would be, including whether there were potential polymorphs, solvates and hydrates of that crystal from;
>
> (d) if there were potential polymorphs, solvates and hydrates, under what conditions those polymorphs, solvates and hydrates could be prepared; and
>
> (e) what the properties of any polymorphs, solvates and hydrates would be.

83. Therefore, even if potential solid forms are discovered, such forms may be unsuitable for formulation and/or manufacture into a drug product and therefore, unsuitable for drug development. Properties such as hygroscopicity, solubility, solid state stability, chemical stability and crystal shape (among others) can all influence the suitability of a solid forms.

84. As summarized by a publication contemporary to the date of the 668 Patent, "the relevance of polymorphism is clear but remains a subject that is not fully or widely understood at a fundamental level." The inherent unpredictability of crystalline solid form was acknowledged in the scientific literature:

> It is still not possible to predict with any reasonable level of confidence the crystal structure of an organic material... The range and combinations of crystal growth conditions are virtually infinite, and there is no way to guarantee the preparation of additional polymorphs of a substance, much less the generation of 'all' of them.

This statement from 1993 remains true, even today. Other references contemporary to the 668 Patent similarly highlight the unpredictability of developing polymorphs.

[Emphasis added, citations omitted.]

[197] Teva argues that the common general knowledge of the Skilled Person had additional elements. A salt form is often preferable to a free base for reasons including crystallinity, solubility, hygroscopicity, stability, and process profile. I accept these submissions, but I also accept the concluding words of the paragraph of the 668 Patent relied on by Teva which states: "[T]he identification of a salt form that exhibits a suitable combination of properties can be difficult." Teva asserts as part of the common general knowledge a point Pfizer itself stated namely that a salt of a compound is generally expected to be more soluble than the free base of the same compound.

[198] Teva further asserts that it was known that such increased solubility "will also improve bioavailability" in circumstances where solubility is poor or rate limiting [my emphasis]. However, I prefer to accept the evidence Teva obtained in cross-examination of Pfizer's Dr. Polli to the effect that what was known was merely that in "some circumstances improving solubility could increase bioavailability" [my emphasis] where dissolution is rate limiting.

[199] Teva says that salt selection strategies and procedures were well known, that regulatory authorities required testing for stability and polymorphism, and a simple preliminary study will normally show the presence of a stable hydrate. I prefer the evidence of Dr. Jamali which was that only properties, such as melting point, stability, and polymorphism had to be tested to be determined. Teva overlooks the fact that research and empirical study was also known to be required as I have found above; in my view the Skilled Person would know that a research program driven by as yet undiscovered empirical data would be necessary if indeed anything of merit in this connection might even be found.

[200] I agree that salt selection was a procedure known in general terms at the time.

[201] In terms of regulatory authorities and their requirement for testing, this again is more complex that asserted by Teva. It was detailed by Pfizer's Dr. Myerson in cross-examination by Teva, and relied on by Teva, whose evidence I accept in this respect. Dr. Myerson testified that FDA guidance "actually required a detailed polymorphism study be done at conditions related to the final isolation step of the API. There is no FDA requirement that you do an extensive polymorph screen to try to find every possible form. What they're really interested in is what forms might exist at the types of conditions you're using in your final isolation and are you aware of them and can you control your process. And then secondarily, any forms that you've identified, were they stable on and that in many cases regulatory authorities required testing for stability and polymorphism before a drug could be put on the market." [Emphasis added.]

[202] Teva says further that the skilled person would attempt to identify the most stable form of a compound; I agree but accept what Dr. Jamali added in cross-examination, namely that for various reasons drug developers eliminate hydrated forms or solvated forms. And so they would pick the most stable non-solvated form.

[203] Teva then asserts that stability testing, I would call them studies and research, involves testing for stability and hygroscopicity (water uptake). I agree, noting that there are different ways to study the matter of hygroscopicity as Dr. Chyall testified on cross-examination.

[204] Teva further asserts that hydrated forms are often preferred because they are generally less likely to be hygroscopic, and therefore may be more stable, which I accept. I accept that hydrates should be identified early on to avoid having to repeat testing.

[205] But these factors simply confirm possibilities for research.

[206] Given that as of 2001, neither ODV succinate nor any of its forms or properties were known including the Form I ODV succinate, in my respectful view, a Skilled Person could not have known, anticipated or predicted the properties of either ODV succinate generally, or Form I ODV succinate, or in particular, whether those properties would be amenable to formulation as a sustained release dosage form, let alone one with any specific pharmacokinetic profile.

[207] The facts of the matter were stated in Dr. Myerson's conclusion which bears repeating:

> 82. Overall, given a particular compound, a person skilled in the art in the early 2000s would not be able to predict:
>
> (a) whether he or she would be able to make any crystal form of that compound;
>
> (b) if so, what level of effort would be required to obtain it;
>
> (c) what its properties would be, including whether there were potential polymorphs, solvates and hydrates of that crystal from;
>
> (d) if there were potential polymorphs, solvates and hydrates, under what conditions those polymorphs, solvates and hydrates could be prepared; and
>
> (e) what the properties of any polymorphs, solvates and hydrates would be.

> 83. Therefore, even if potential solid forms are discovered, such forms may be unsuitable for formulation and/or manufacture into a drug product and therefore, unsuitable for drug development. Properties such as hygroscopicity, solubility, solid state stability, chemical stability and crystal shape (among others) can all influence the suitability of a solid forms [sic].
>
> 84. As summarized by a publication contemporary to the date of the 668 Patent, "the relevance of polymorphism is clear but remains a subject that is not fully or widely understood at a fundamental level." The inherent unpredictability of crystalline solid form was acknowledged in the scientific literature:
>
> > It is still not possible to predict with any reasonable level of confidence the crystal structure of an organic material... The range and combinations of crystal growth conditions are virtually infinite, and there is no way to guarantee the preparation of additional polymorphs of a substance, much less the generation of 'all' of them.
>
> This statement from 1993 remains true, even today. Other references contemporary to the 668 Patent similarly highlight the unpredictability of developing polymorphs.

G. Identify the inventive concept of the claim in question or if that cannot readily be done, construe it

[208] Identifying the inventive concept is the next step in the obviousness analysis outlined by the Supreme Court in *Sanofi*. The Federal Court of Appeal in *Atanazavir* held that the "inventive step" is the same as "the solution taught by the patent." In this connection, having regard to the Federal Court of Appeal's comments concerning *Beloit*, and the decision of the Supreme Court in *Sanofi*, in my respectful view "what is claimed in the patent" and "the invention" are synonymous with "inventive step" and "the solution taught by the patent."

[209] This second point, the solution taught by the patent, also known as the inventive concept is to be assessed in respect of each claim at issue: *Sanofi* at para 67. I accept that different claims may have different inventive concepts, and as Teva's expert Dr. Fiese testified, a crystal form claim may have a different inventive concept than a salt form claim. Dr. Fiese in cross-examination agreed that: "crystalline forms can have inventive concepts that are separate from the inventive concept of the salt." See also: *Pozzoli Spa v BDMO*, [2007] FSR 37 (2007) at para 17:

> What now becomes stage (2), identifying the inventive concept, also needs some elaboration. As I pointed out in *Unilever Pie v Chefaro Proprietaries Ltd* [1994] R.P.C. 567 at 580:
>
> > "It is the inventive concept of the claim in question which must be considered, not some generalised concept to be derived from the specification as a whole. Different claims can, and generally will, have different inventive concepts."

i. Claims 8 and 9

[210] Both of Claims 8 and 9 cover Form I ODV (mono) succinate monohydrate, that is, the crystalline form of ODV succinate. Claims 8 and 9 specifically claim a new and distinct composition of matter. Claim 8 says this crystal form exhibits a fingerprint, namely characteristic XRPD as set out in Figure 1, while Claim 9 identifies another fingerprint namely that the polymorph crystal exhibits a characteristic endotherm (melting point) at about 131°C. In my view, these identification or characterization data, which are inherent to the form of the novel crystal at issue, are not the invention; these properties are not the inventive concept, nor are they the solution taught by the 688 Patent.

[211] In my respectful view, the solution taught by these two claims, their inventive concept, is the novel crystalline form of ODV succinate referred to as Form I. In short, the inventive concept or the solution taught by the 668 Patent is the novel crystal Form I ODV succinate.

[212] In its affidavit material Teva advances an over-arching inventive concept that applies to all the relevant 668 Patent's claims. Teva's Dr. Fiese said: "the skilled person would construe the inventive concept of the 668 Patent (including all of Claims 1-2, 4-9, 20-21, 23-33, and 43-44), as 0-desmethyl-venlafaxine ("ODV") succinate and its improved physicochemical and pharmacokinetic properties, when compared with other forms of ODV." Teva's Dr. Jamali deposed that Claims 1, 43 and 44 had the same inventive concept. Dr. Lieberman said the inventive concept was the same for all the claims, namely that: "… ODV succinate, having superior chemical and pharmacokinetic properties compared to other ODV salts and free base."

[213] However, Dr. Fiese in cross-examination agreed not only that "crystalline forms can have inventive concepts that are separate from the inventive concept of the salt", but later in his affidavit deposed "[C]laim 33 claims the use of ODV succinate for the treatment of depression", and that "[C]laims 43 and 44 are directed to the use of sustained release dosage forms or formulations of ODV succinate to provide a specified blood plasma or serum level of no more than 225 ng/ml." On the claims at issue now, 8 and 9, Dr. Fiese agreed in cross-examination with Pfizer's counsel that "insofar as Claims 4 to 9 cover various solid state forms of ODV succinate, you recognize that they could have additional inventive concepts associated with them?"

[214] No doubt all five claims in issue relate to Claim 1, which is not asserted; Claim 1 is to the salt form of ODV succinate ("[A] compound which is O-desmethyl-venlafaxine succinate or a mixed salt thereof."

[215] However, given this evidence particularly the evidence of Teva's Dr. Fiese on cross-examination, I do not agree that there is an over-arching inventive concept or solution taught by the invention applicable to all five claims in issue.

ii. Claim 33

[216] Claim 33 depends on Claims 8 and 9. Claim 33 states: "[U]se of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one claims 1 to 20 for the treatment of depression." This is a use claim, and in the context of this litigation, is a claim to the use of an effective amount of Form I ODV (mono) succinate monohydrate that is, to the use of an effective amount of the crystalline form of ODV succinate for the treatment of depression.

[217] I am unable to agree that the 'overarching' claim as alleged by Teva's witnesses applies to Claim 33 any more than such an overarching claim might apply to Claims 8 and 9. Such an interpretation is not consistent with the evidence, nor with how I construe Claim 33 which is written clearly. I see no reason to depart from its plain meaning modified only to acknowledge that its inventive concept, or what the 668 Patent teaches in this respect, must be considered within the context of my findings with respect to Claims 8 and 9 on which it depends.

[218] Therefore, the inventive concept or solution taught by Claim 33 is the use of an effective amount of the crystalline Form I ODV (mono) succinate monohydrate for the treatment of depression.

iii. Claim 43

[219] Claim 43 is expressed: "[U]se of therapeutically effective amount of sustained release oral dosage form comprising O-desmethyl;-venlafaxine succinate or a mixed salt thereof as claimed in any one of Claims 1 to 20 prepared in a dosage to induce a blood plasma level no more than 225 ng/ml to lower the incidence of nausea, vomiting, diarrhea, abdominal pain, headache, vaso-vagal malaise, or trismus resulting from the oral administration of O-desmethyl-venlafaxine succinate."

[220] As noted there is no substantial disagreement on the construction of Claim 43. In addition I have found there is no overarching claim which finding applies to Claims 43 and 44.

[221] The inventive concept of Claims 43 and 44 is a sustained release dosage form comprising the new salt, ODV succinate (or Form I ODV succinate, as those claims depend on Claims 8 or 9) that has specific pharmacokinetic characteristics (a peak blood plasma level of less than 225 ng/ml and), and therefore reduces the incidence of certain side effects that would otherwise result from oral administration of ODV succinate.

iv. Claim 44

[222] Claim 44 is made as follows: "[A] sustained release formulation comprising O-desmethyl-venlafaxine succinate and a pharmaceutically acceptable carrier or excipient, wherein the sustained release formulation provides peak serum levels of up to 225ng/ml."

[223] The parties agree on the construction of Claim 44, as follows:

Claim 44 Pfizer construction	Claim 44 Teva construction
A sustained release formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I ODV succinate) which provides average peak serum levels up to 225 ng/ml.	A sustained released formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I OCD succinate) which provides peak serum levels of up to 225 ng/ml.

[224] In my respectful opinion, the inventive concept and solution taught by the invention in Claim 44 is a sustained release formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I ODV succinate) which provides average peak serum levels up to 225 ng/ml.

[225] Taken together, the evidence of Pfizer's Dr. Polli, which I accept, is that the inventive concept of Claims 43 and 44 is a sustained dosage form comprising the novel salt, ODV succinate (or Form I ODV succinate, as those claims depend on Claims 8 or 9) that has specific pharmacokinetic characteristics (a peak blood plasma level of less than 225 ng/ml), and therefore reduces the incidence of certain side effects that would otherwise result from oral administration of ODV succinate. The difference between the two is that Claim 43 references lowering the

incidence of adverse side effects while Claim 44 does not; both refer to a peak blood plasma level of less than 225 ng/ml.

H. Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed

[226] I will take this stage of the analysis on a claim by claim basis.

i. Claims 8 and 9

[227] In my respectful view, and as the experts agree, it would not have been possible at the relevant time for a Skilled Person to predict whether ODV succinate salt would form as a solid, whether that solid would be crystalline, or what the properties of any hypothetical crystalline solid would be. This is the case regardless of the fact that salt screens were generally known as were, also in general terms, crystallization and polymorph screens. In fact, neither ODV succinate nor any of its crystalline forms, let alone Form I, were specifically previously disclosed in the art.

[228] The solution taught by Claims 8 and 9, their inventive concept, is the novel crystalline form of ODV succinate referred to as Form I. In short, the inventive concept or the solution taught by the 668 Patent is the novel crystal Form I ODV succinate.

[229] The gap between the state of the art and the inventive concept of Claims 8 and 9 of the 668 Patent is therefore the invention of a new composition of matter namely Form I ODV succinate.

ii. Claim 33

[230] To recall, the inventive concept or solution taught by claim 33 is the use of an effective amount of the crystalline Form I ODV (mono) succinate monohydrate for the treatment of depression. Claim 33 depends on Claims 8 and 9.

[231] Teva says that Claim 33 discloses no further inventive step over Claims 8 and 9. I agree with Pfizer that the Skilled Person would know that ODV as the metabolite of venlafaxine was useful in the treatment of depression. However, the prior art also taught that every new solid form had its own set of unknown, unpredicted and unpredictable properties.

[232] Pfizer says that because the prior art did not disclose the Form I ODV succinate or for that matter, any of its properties, the gap between the prior art and invention of Claim 33, the use of this novel crystalline form for the treatment of depression, was not obvious. I agree.

[233] In addition, and in my view for the same reasons that Form I was not more or less self-evident, neither was its use to treat depression.

[234] The gap between the state of the art and the inventive concept of Claim 33 of the 668 Patent is therefore the invention of a new composition of matter namely Form I ODV succinate to treat depression.

iii. Claim 43 and 44

[235] In terms of Claims 43 and 44, both depend on Claims 8 and 9 *i.e.*, the crystalline Form I ODV succinate. To recall, the inventive concept of Claims 43 and 44 is a sustained release dosage form comprising the novel salt, ODV succinate (or Form I ODV succinate, as those claims depend on Claims 8 or 9) that has specific pharmacokinetic characteristics (a peak blood plasma level of less than 225 ng/ml).

[236] Claim 43 in addition to the foregoing, claims a reduction in side effects over the oral administration of Form I ODV succinate in an immediate release formulation; both reference a peak blood plasma level of less than 225 ng/ml, but Claim 44 does not refer to side effects.

[237] Pfizer says that the gap between the prior art and Claims 43 and 44 is the invention of a new sustained release dosage form of the novel salt or crystalline form that reduces blood plasma levels of ODV and reduces the incidence of adverse events from the non-sustained release administration. With respect, I agree.

[238] I have found that neither ODV succinate nor any of its forms or properties were known, predicted or predictable. Therefore the Skilled Person could not anticipate what properties either ODV succinate or Form I ODV succinate would have, which means that the Skilled Person could not anticipate whether those properties would allow the formulation of a sustained release dosage. As noted in Claim 33, the prior art taught and the Skilled Person knew that every new solid form had its own set of unknown, unpredicted and unpredictable properties.

[239] In addition, for the same reasons that Form I was not more or less self-evident, neither was its use in sustained release formulation. Likewise it cannot be said that the use of Form I ODV succinate in sustained release formulation was more or less self-evident to reduce adverse side effects.

[240] Teva notes that the prior art disclosed that sustained release formulations of other drugs including EFFEXOR XR had been both made and used to ameliorate blood plasma concentrations generated by immediate administration, and I agree. But the prior art contained no application of this general principle to ODV, nor to ODV succinate nor to Form I ODV succinate. The evidence establishes that it would not have been obvious to the Skilled Person that ODV succinate had any stable, solid crystal form at all, let alone one that could be formulated into a SR formulation. Nor was it obvious or predicted or predictable that ODV succinate Form I would have the appropriate solubility, permeability and bioavailability characteristics for oral formulation development as identified by the experimentation entailed in its development. It was not known, predicted or predictable that any such SR formulation of ODV succinate would result in blood plasma levels below 225 ng/ml which maintaining therapeutic concentrations as per both Claims 43 and 44.

[241] Teva also says the 225 ng/ml ratio is arbitrary, which argument I rejected above at para 114. The evidence is that specific Cmax threshold was derived [redacted]

I. Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

i. Apply the definition of obvious before *Sanofi*

[242] At this point in the analysis, in light of *Atanzavir* and instead of moving next to an 'obvious to try' analysis, I will apply the test for obviousness set out by the Federal Court of Appeal in *Beloit*.

[243] Thus, the question becomes whether the Skilled Person would, in the light of the state of the art and of common general knowledge as at the claimed date of invention, have come directly and without difficulty to the solution taught by the patent, namely directly and without difficulty to the novel crystalline form of ODV succinate referred to as Form I. In my respectful view, the evidence does not justify such a conclusion.

[244] I appreciate Teva's arguments to the effect that its witnesses were blinded, but that is a question of relevance, reliability and weight: *Gilead Sciences, Inc v Canada (Health)*, 2016 FC 857 at para 59, and see the cases discussed there. In the end, I prefer the evidence of Dr. Myerson on the common general knowledge regarding Claims 8 and 9. Dr. Myerson was a professor of Industrial Pharmacy and Pharmaceutics, and his evidence was credible and comprehensive in this connection. I have also accepted the evidence of Dr. Park based on her experience in this connection, see para 129 and following of these Reasons, which corroborates that of Dr. Myerson. Dr. Myerson deposed:

57. The salt selection and formation process is highly unpredictable. Indeed, one cannot predict prior to actually attempting to form a salt whether the reaction of a given active drug compound with particular acid or base will successfully produce a salt or what the properties of that salt will be.

58. Once a salt form is found with particular counterion, that salt is another set of experiments conducted over a variety of different conditions to determine what, if any, crystalline forms exist for that particular salt.

59. The solid form of a particular salt form can significantly influence a number of physical and chemical properties of the API including solubility, dissolution rate, chemical stability, hygroscopicity, crystal shape and manufacturing/processing characteristics. Scientists cannot predict how the formation of a particular solid form of salt will affect these properties prior to successful formation and analysis of the salt and its solid forms. Therefore, it is no possible to predict in advance of actually making the salt whether its formation will yield any solid form (crystalline or amorphous), much less one with desirable properties that those of the free base or other salt forms of the drug.

…

67. Some chemical species can crystallize into more than one three-dimensional crystal structure. This phenomenon is called polymorphism (or allotropism if the species is an element such as carbon). While polymorphism is relatively common among organic molecules, whether or not a particular compound is capable of polymorphism – and if so how many different polymorphs may exist – cannot be predicted and must be determined empirically (to the extent possible to do so).

…

72. Pseudo-polymorphism refers to the ability of certain compounds to crystallize in a structure that contains a solvent as part of the crystal lattice. These crystals are also known as solvates. A solvate in which the solvent is water is usually referred to as a hydrate. For a given pseudo-polymorph, the ratio of the number of molecules of solvent to the number of molecules of the chemical species itself is usually fixed. This is referred to as its stoichiometry. These forms are referred to as pseudo-polymorphs because although they involve the same compounds, they also include solvent molecules as part of the structure.

…

76. Like the different polymorphs of given compound, it is also not possible to predict in advance whether or not a compound may have one or more pseudo-polymorphs and if so, what those pseudo-polymorphs may be. Knowledge of the existence of polymorphs or pseudopolymorphs for one compound does not provide useful information about the existence of polymorphs or pseudopolymorphs of a different compound (even if the compounds are structurally similar, or are different salts of the same molecule).

…

80. Today, the research for crystalline forms, including polymorphs, solvates and hydrates, has become a significant part in the development of new pharmaceutical products. Polymorph screening is time consuming with no ability to predict success in identifying a suitable solid-state form for development. Solid form screening for a given compound can involve thousands of experiments performed over many months or even longer. There is no "standard" method for performing a solid form screen and the number of experiments and conditions that are tried are depending on the choices made by the investigator and the time allotted to the screen.

[245] Dr. Myerson concluded:

81. While the general methods to perform crystallizations at different conditions and with different solvents were known in the art as of the early 2000s, there are a wide variety of combinations of variables such as, solvents, solvent mixtures, temperatures, cooling rates, evaporation rates, etc. that could be used to attempt to generate new solid state forms. Thus, the number of potential experiments that can be conducted is extremely large.

82. Overall, given a particular compound, a person skilled in the art in the early 2000s would not be able to predict:

(a) whether he or she would be able to make any crystal form of that compound;

(b) if so, what level of effort would be required to obtain it;

> (c) what its properties would be, including whether there were potential polymorphs, solvates and hydrates of that crystal form;
>
> (d) if there were potential polymorphs, solvates and hydrates, under what conditions those polymorphs, solvates and hydrates could be prepared; and
>
> (e) what the properties of any polymorphs, solvates and hydrates would be.

83. Therefore, even if potential solid forms are discovered, such forms may be unsuitable for formulation and/or manufacture into a drug product and therefore, unsuitable for drug development. Properties such a hygroscopicity, solubility, solid state stability, chemical stability and crystal shape (among others) can all influence the suitability of a solid form.

84. As summarized by a publication contemporary to the date of the 668 Patent, "the relevance of polymorphism is clear but remains a subject that is not fully or widely understood at a fundamental level." The inherent unpredictability of crystalline solid form was acknowledged in the scientific literature:

> It is still not possible to predict with any reasonable level of confidence the crystal structure of an organic material …. The range and combinations of crystal growth conditions are virtually infinite, and there is no way to guarantee the preparation of additional polymorphs of a substance, much less the generation of 'all' of them.

This statement from 1993 remains true, even today. Other references contemporary to the 668 Patent similarly highlight the unpredictability of developing polymorphs.

[246] In my respectful view, the Skilled Person, in the light of the state of the art and of common general knowledge as at the claimed date of invention as just outlined, would not have come directly and without difficulty to the solution taught by the patent, namely the novel crystalline form of ODV succinate referred to as Form I.

[247] In this connection, the experts agree that it would have been impossible at the relevant time for a Skilled Person to predict whether the ODV succinate salt would form as a solid, whether that solid would be crystalline, or what the properties of a hypothetical crystalline solid would be.

[248] To recall, the test in *Beloit* is whether the Skilled Person would "in the light of the state of the art and of common general knowledge as at the claimed date of invention, have come directly and without difficulty to the solution taught by the patent." This test is not met on the facts of this case. In my respectful view, the road seen by the Skilled Person based on the prior art would be difficult and not direct. The Skilled Person would foresee an extremely large number of studies and tests with no identified or predictable result.

[249] In essence the Skilled Person would see a research program. This finding applies to Claims 8 and 9. As they are dependent on Claims 8 and 9, those findings apply equally to Claims 33, 43 and 44 as outlined above.

[250] The obviousness inquiry does not end here. At this point, having looked at obviousness as set out in *Atazanavir* and *Beloit*, the Court must follow the balance of the steps as suggested by *Sanofi*. The Court must now consider the applicability of, and if appropriate, review the matter against the 'obvious to try' test.

ii. Consider the doctrine of obvious to try

[251] As the Supreme Court noted at para 67 of *Sanofi*, "[I]t will be at the fourth step of the Windsurfing/Pozzoli approach to obviousness that the issue of 'obvious to try' will arise." Having said that the Supreme Court asked: "When Is the 'Obvious to Try' Test Appropriate?" In answer at para 68 it said: "[I]n areas of endeavour where advances are often won by experimentation, an "obvious to try" test might be appropriate. In such areas, there may be numerous interrelated variables with which to experiment. For example, some inventions in the pharmaceutical industry might warrant an "obvious to try" test since there may be many chemically similar structures that can elicit different biological responses and offer the potential for significant therapeutic advances."

[252] This case falls into the "pharmaceutical industry" category; therefore the next step is to consider the factors discussed by the Supreme Court in *Sanofi*, recognizing that they are not exhaustive.

[253] In doing so regard must be had to the Supreme Court's introductory comments: "[H]owever, the 'obvious to try' test must be approached cautiously. It is only one factor to assist in the obviousness inquiry. It is not a panacea for alleged infringers. The patent system is intended to provide an economic encouragement for research and development. It is well known that this is particularly important in the field of pharmaceuticals and biotechnology." These were said to be "useful guidance" by the Federal Court of Appeal in *Pfizer v Apotex*, 2009 FCA 8 at para 26.

[254] These Reasons will consider the obvious to try analysis first without reference to this guidance, and then come back to them to determine what if any difference they make to the analysis; in the manner proposed it will be easier to determine the impact of this guidance on the Court's conclusions.

[255] After establishing this guidance in *Sanofi*, the Supreme Court set out factors that should be considered:

> [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.

[256] I will deal with each of these considerations.

J. 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?

[257] The parties disagree. Both parties cited cases where, on the accepted evidence in a particular case, courts came to conclusions on obvious to try one way or the other. While of relevance, each case in this connection has been decided on facts particular to it, and having regard to the submissions of the experts and counsel. None of the cases say that all salt screens are obvious to try, or are 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 this is a question of applying the law of obvious to try to the evidence before the Court.

[258] Pfizer says that all the experts agree that the existence and properties of crystal forms cannot be predicted in advance of their having been successfully made and tested. A Skilled Person would not know nor could he or she predict that Form I ODV succinate existed nor could they identify or predict what properties it would have, or how if at all, it could be prepared. In my respectful view this is an accurate summary.

[259] This summary is borne out in the extracts from the affidavit of Dr. Myerson referred at paras 196, 244 and 245. This evidence at least insofar as polymorph and crystal screening is concerned is corroborated by Dr. Park's experience as set out at para 129 and following of these reasons. Dr. Myerson concluded with respect to the crystallization and polymorph screening:

> 82. Overall, given a particular compound, a person skilled in the art in the early 2000s would not be able to predict:

> (a) whether he or she would be able to make any crystal form of that compound;
>
> (b) if so, what level of effort would be required to obtain it;
>
> (c) what its properties would be, including whether there were potential polymorphs, solvates and hydrates of that crystal from;
>
> (d) if there were potential polymorphs, solvates and hydrates, under what conditions those polymorphs, solvates and hydrates could be prepared; and
>
> (e) what the properties of any polymorphs, solvates and hydrates would be.
>
> 83. Therefore, even if potential solid forms are discovered, such forms may be unsuitable for formulation and/or manufacture into a drug product and therefore, unsuitable for drug development. Properties such as hygroscopicity, solubility, solid state stability, chemical stability and crystal shape (among others) can all influence the suitability of a solid form.
>
> 84. As summarized by a publication contemporary to the date of the 668 Patent, "the relevance of polymorphism is clear but remains a subject that is not fully or widely understood at a fundamental level." The inherent unpredictability of crystalline solid form was acknowledged in the scientific literature:
>
> > It is still not possible to predict with any reasonable level of confidence the crystal structure of an organic material... The range and combinations of crystal growth conditions are virtually infinite, and there is no way to guarantee the preparation of additional polymorphs of a substance, much less the generation of 'all' of them.

[260] Pfizer's summary of what the Skilled Person would know is to my mind confirmed by the cross-examination of Teva's expert Dr. Fiese. Relevant extracts include:

> 420 Q. Okay. We'll come back to that. You'd agree with me, Dr. Fiese, that you can't predict in advance whether a particular salt of a compound will form a crystalline salt?

A. That's correct.

421 Q. You also can't predict what the other properties of that salt might be?

A. That's correct.

660 Q. You don't know whether ODV tartrate has a crystalline monohydrate form, do you?

A. No.

661 Q. And you don't know whether ODV maleate has a crystalline monohydrate form?

A. No.

689 Q. In your view, a skilled person has an expectation that they will find a salt with suitable solubility if they conduct a salt screen?

A. Yes

690 Q. But a skilled person is not going to know which salt that is going to be in advance?

A. No, not in advance.

691 Q. And they're not going to know how many salts they're going to need to make before they find it?

A. That's correct.

847 Q. If we go back to your affidavit, I would like to turn paragraph 113. In paragraph 113 you say a skilled person would have expected that one or more of the ODV salts identified in the U.S. '186 and WO 851 patent would be suitable for use in a solid oral dosage form?

A. Yes.

848 Q. What the skilled person could not have expected is which salt that would be?

A. That's correct.

850 Q. So we know now that ODV succinate is a suitable salt of ODV?

A. Yes.

851 Q. But a person skilled in the art in February 2001 wouldn't have known that?

A. They would have known fumarate would work. They would have been encouraged to stay in that family but they wouldn't have known specifically if succinate worked.

861 Q. And so this statement that the skilled person would readily determine that ODV succinate would be one such suitable salt, again, that is the statement that you're making with the benefit of hindsight?

A. You also knew the fumaric was going to work, so the prior art would tell you that you want to go in that area.

862 Q. Right.

A. So it's not an after-the-fact thing; it was more of a prior thing.

863 Q. Right, but the knowledge that ODV is a suitable salt that works is knowledge we have now?

A. Yes.

864 Q. It's not knowledge a skilled person would have in 2001?

A. Not before they made it, no.

872 Q. In 2001 it would not have been possible to predict how many crystalline forms a compound had?

A. That's correct.

873 Q. Or what they would be?

A. That's correct.

877 Q. When you say it would be obvious to try to make and characterize that form, you'd agree with me a skilled person as of 2001 doesn't know that Form I exists, correct?

A. I think that's correct.

878 Q. So I think what you mean here is a skilled person would be motivated to try to generate crystalline solids of ODV succinate?

A. Yes.

879 Q. And they would be motivated to try to identify a crystalline solid that was stable at ambient conditions?

A. Right.

880 Q. So what you're saying is that in doing that they may arrive at Form I?

A. Right.

881 Q. But they could not predict in advance that Form I existed?

A. No.

882 Q. Or what its properties would be?

A. No, they couldn't.

883 Q. Or what its characteristics would be, like its XRPD pattern?

A. That's correct.

884 Q. As of 2001 if you had asked a skilled person to describe a stable crystalline form of ODV succinate they could not have done that?

A. No. You knew the properties you wanted to have, but does succinate have it? No idea.

885 Q. Right. And you don 1 t know that there ' s going to be a particular crystal form with the XRPD pattern set out in Claim 8 that's going to satisfy that requirement?

A. No.

886 Q. And I think we had talked about the generation of different salts using different conditions, but I 'm right that different conditions can also result in different solid state forms?

A. Oh yeah.

887 Q. So if I vary the conditions of my crystallization experiment I can get one solid state form versus another solid state form of the same compounds?

A. So if I vary the conditions of my crystallization experiment I can get one solid state form versus another solid state form of the same compounds?

888 Q. And these conditions that I would vary would include things like solvent?

A. Yes.

889 Q. Temperature?

A. Yes.

890 Q. Prescription method?

A. Yes.

891 Q. Timing?

A. Timing, yes.

892 Q. Humidity?

A. Probably not.

893 Q. Or presence of water?

A. Presence of water.

894 Q. Degree of mixing?

A. Yes.

895 Q. And the form that is going to result from any given crystallization experiment is going to depend on those conditions that I select?

A. Correct.

896 Q. And that's not something I can predict in advance?

A. No.

897 Q. Empirical?

A. Yes.

[261] In my respectful view, this evidence of Dr. Fiese contradicts what he deposed in his affidavit. In my view this contradictory evidence considerably weakens his evidence. In his affidavit, Dr. Fiese deposed:

> 114. I do not agree with Dr. Chyall's assertion (paragraph 44) that:
>
> > A skilled person would have no way to predict what amount of effort, conditions or experiments would be required to reach any salt form of ODV, or that any particular salt could be made successfully or would have properties that would be suitable for formulation.
>
> 115. Similarly, Dr. Myerson states (paragraph 42) that: "It could not have been more or less self-evident to a skilled person that any particular salt of ODV (including succinate) could be made... " and that "a skilled person could not have predicted that any particular salt of ODV (including succinate) would have properties that would make it suitable for formulation in advance of actually making and testing it."
>
> 116. This dramatically overstates the uncertainty involved in the process by presuming that the skilled person must pick a suitable salt before testing any of the salts. In pharmaceutical science, there is never a guarantee of success, or a guarantee that things will be easy. However, in the case of ODV, it is my opinion that the skilled person would be confident that a suitable salt form could be identified with a routine salt screen. The skilled person would readily determine that ODV succinate would be one such suitable salt. Dr. Shah's affidavit confirms that this was in fact.
>
> [Emphasis in original.]

[262] In this connection, I note that Dr. Fiese's answers to question 863 and 864 support Pfizer's contention that Dr. Fiese's affidavit evidence relied on impermissible hindsight regarding the ODV succinate salt. In the circumstances I accept Dr. Fiese's testimony on cross-examination over that deposed in his affidavit.

[263] Based on this evidence I conclude that it was not more or less self-evident to the Skilled Person that what is being tried, namely the crystalline Form I ODV succinate, ought to work. This is the evidence of Dr. Myerson, and in my view it is confirmed in material ways by Dr. Fiese. In summary, I find that the crystal form of Form I ODV succinate was not more or less self-evident to the Skilled Person.

[264] The second part of this question asks whether there are a finite number of "identified predictable solutions" known to persons skilled in the art; in my view this was not the case because the number of potential experiments was in fact extremely large. That was the evidence of Dr. Myerson which I accept who deposed that "the number of potential experiments that can be conducted is extremely large":

> 80. Today, the research for crystalline forms, including polymorphs, solvates and hydrates, has become a significant part in the development of new pharmaceutical products. Polymorph screening is time consuming with no ability to predict success in identifying a suitable solid-state form for development. Solid form screening for a given compound can involve thousands of experiments performed over many months or even longer. There is no "standard" method for performing a solid form screen and the number of experiments and conditions that are tried are depending on the choices made by the investigator and the time allotted to the screen.
>
> 81. While the general methods to perform crystallizations at different conditions and with different solvents were known in the art as of the early 2000s, there are a wide variety of combinations of variables such as, solvents, solvent mixtures, temperatures, cooling rates, evaporation rates, etc. that could be used to attempt to generate new solid state forms. Thus, the number of potential experiments that can be conducted is extremely large.
>
> [Emphasis added.]

[265] This fact was confirmed by Dr. Park's experience who deposed at para 31 of her affidavit that SSCI typically conducted a "large number of different experiments under a wide variety of conditions in order to try to identify as many different solid state forms as possible."

[266] I also note the Supreme Court in *Sanofi* poses the question as one concerning "identified predictable solutions." While there were research possibilities, and the possibility of conducting studies, and indeed the possibility of engaging on a research program, in my respectful view on the facts of this case there were no identified predictable solutions.

[267] Teva argues that because salt screens and polymorph tests, among other things, were generally known in the prior art, it would be more or less self-evident to the Skilled Person that Form I ODV succinate, *i.e.*, what is being tried, ought to work. I disagree. A general knowledge of salt screens and what was known of polymorph tests merely provided possibilities for conducting research, studies and further experiments which in this case was in the nature of a research program. This is not enough; every Court that has reviewed this matter has agreed that mere possibilities do not satisfy the obvious to try set out in *Sanofi*.

[268] In my view, the fact of certain known tests and procedures in this case is very analogous to the facts before the Supreme Court in *Sanofi*, where the second person advanced similar arguments that were rejected. The Court, in rejecting arguments like those of Teva here, stated:

> [85] Just because there are known methods of separating a racemate into its isomers does not mean that a person skilled in the art would necessarily apply them. <u>The fact that there are such known methods of separation will be of no account if the evidence does not prove that it was more or less self-evident to try them.</u> It is true that at the relevant time there was evidence that a skilled

> person would know that the properties of a racemate and its isomers might be different. However, a possibility of finding the invention is not enough. The invention must be self-evident from the prior art and common general knowledge in order to satisfy the "obvious to try" test. That is not the evidence in this case.
>
> [Emphasis added.]

[269] In my respectful view this is the situation here: salt screens and the availability of crystallization and polymorph screening were generally known as methods by which it might be possible to screen for salts, which may or may not solidify, with any such resulting salts having unknown and unpredictable properties. It was also known to the Skilled Person that through crystallization and polymorph screening it might be possible to identify crystals and polymorphs, but the Skilled Person would also know that no such crystal or polymorph forms might be possible, and that even if any crystals or polymorphs were found, they would have unknown and unpredictable properties. In my view that does not make the inventive concept of the Claims 8 and 9, namely, Form I ODV succinate, obvious to try. In my view these were mere possibilities of identifying the ODV succinate salt, or perhaps no salt at all, in a salt screen in first instance, and a possibility of finding Form I ODV succinate crystalline, or perhaps no crystalline form at all, in crystallization and polymorph screening in the second place. Again, mere possibilities are not sufficient.

[270] Routine experimentation is permitted under the obvious to try analysis. The issue of routine experimentation was recognized by the Federal Court of Appeal in *Plavix 2* at para 81, and is referenced in *Sanofi* itself under the second question in obvious to try. But I disagree with the position advanced by Teva that this makes the present invention one that was obvious to try; in my view far more than routine experimentation would have been foreseen by the Skilled

Person in this case. A general knowledge of salt screens and what was known of crystallization and polymorph screening, merely provided possibilities for the Skilled Person to conduct research, studies and further experiments which in this case were significant and in the nature of a research program particularly in the area of crystallization and polymorph screening. This is not enough; every Court that has reviewed this matter has agreed that mere possibilities do not satisfy the obvious to try set out in *Sanofi*.

[271] Another fundamental problem with these arguments is that they are contrary to the expert evidence of Dr. Myerson and the experience of Dr. Park which I have accepted. That aside, even if all of these arguments are accepted as being in the prior art, contrary to my findings, in my view they simply set up the very same situation rejected by the Supreme Court in *Sanofi*:

> [85] Just because there are known methods of separating a racemate into its isomers does not mean that a person skilled in the art would necessarily apply them. The fact that there are such known methods of separation will be of no account if the evidence does not prove that it was more or less self-evident to try them." As Sanofi put it, knowing these procedures existed is of no account because the evidence does not prove it was more or less self-evident to try them: "a possibility of finding the invention is not enough. The invention must be self-evident from the prior art and common general knowledge in order to satisfy the 'obvious to try' test. That is not the evidence in this case.

[272] That is not the evidence in this case either: the invention was not self-evident from the prior art and the common general knowledge on the evidence in this case. I am unable to find that the uninventive and unimaginative Skilled Person would consider the invention was self-evident from the prior art and the common general knowledge.

[273] In my respectful view the situation outlined in *Sanofi* is the situation here: salt screens and the availability of crystallization and polymorph screening were generally known as methods by which it might be possible to screen for salts, which may or may not ,solidify, with any such resulting salts having unknown and unpredictable properties. It was also known to the Skilled Person that through salt screens and crystallization and polymorph screening research programs it might be possible to identify crystals and polymorphs.

[274] However the Skilled Person would also know that no such crystal or polymorph forms might be possible, and that if any crystals or polymorphs were found, they would have unknown and unpredictable properties. In my view that does not make the inventive concept of the Claims 8 and 9, namely, Form I ODV succinate, obvious to try. The evidence in this case established what were mere possibilities of identifying the ODV succinate salt, or perhaps no salt at all, in a salt screen in first instance, and a possibility of finding Form I ODV succinate crystalline, or perhaps no crystalline form at all, in crystallization and polymorph screening. But mere possibilities are not sufficient.

[275] In my view, this head points against a finding of obvious to try in this case.

K. <u>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?</u>

[276] I have accepted the evidence of Dr. Myerson on the extent, nature and amount of effort to achieve the invention as known to the Skilled Person - paras 196, 244 and 245. I also have accepted Dr. Park’s experienced-based evidence on crystallization and polymorph screening –

see above at para 129 and following. In my respectful view, the extent nature and amount of effort required to achieve the invention, that is, to achieve Form I ODV succinate, was considerable; what was needed would be seen by the Skilled Person as a research program.

[277] Again with reference to *Sanofi* at para 86, there is no evidence that at the relevant time a Skilled Person 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 is 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 the other would now work. [redacted] The nature of the work seen in this context was uphill.

[278] Also by analogy to *Sanofi*, at para 87, there was no evidence that at the relevant time the Skilled Person would know the properties of ODV succinate, nor would the Skilled Person have known or predicted the properties of the novel crystalline form claimed in the 668 Patent.

[279] While I agree that salt screening may not have been seen by the Skilled Person as "prolonged and arduous", that is not the case with the crystallization and polymorph screening performed by SSCI which I find would have been seen as difficult and prolonged. In addition, the Skilled Person would see as prolonged and arduous the overall research program that was conducted here, which in my view was justified and reasonable in this drug development context, which included pro-drug experimentation, salt screening and polymorph screening together with the *in vitro* and *in vivo* testing including that [redacted], rats, dogs and humans. While Teva points to a 1994 document in which Pfizer personnel characterized salt formation "as a simple, almost trivial, means of overcoming some undesirable properties e.g. solubility, stability and dosage form manufacturability of the parent drug substance", in my respectful view the invention story considered not in isolated components but as a whole, from the initial pro-drug experiments, the salt selection processes, the exploration of the properties of ODV succinate, SSCI polymorph and crystallization work leading to the discovery of the new crystal forms including Form I ODV succinate, was anything but trivial.

[280] This factor points away from finding obvious to try.

L. Is there a motive provided in the prior art to find the solution the patent addresses?

[281] What is required to establish motivation is whether there is a motive provided in the prior art to find "the solution the patent addresses." The solution the 668 Patent addresses, as found, is the new composition of matter namely crystalline Form I ODV succinate.

[282] 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 Skilled Person would have had no knowledge or predictability of what forms existed nor how they could be formed.

[283] Pfizer's position is that beyond a general statement about the possibility of other pharmaceutically acceptable salts of ODV, there was no pre-existing motive provided in the prior art to find the solution provided by the 668 Patent. It says, and I agree, that while a Skilled Person perhaps would have had a general motive to find a form of ODV that could be formulated, there was no suggestion as to which salts might have crystalline forms. In my view, and in addition, there was no evidence of motivation pointing in the direction of the succinate salt as the solution and certainly no evidence of motivation to prepare any particular solid state form of ODV succinate, let alone Form I ODV succinate which is the solution taught by the 668 Patent.

[284] Again, I look at *Sanofi*, this time at para 90, and note that the Supreme Court examined the facts for evidence that "provided a specific motivation for the skilled person to pursue" the invention claimed. There as here, there is a lack of specific motivation, and I emphasize the words "specific motivation", in the prior art to find the novel crystalline Form I ODV claimed by the 668 Patent.

[285] I note also that *Sanofi* dealt with a genus patent, where, as the Supreme Court stated, "selection might be expected" at para 90, but nonetheless the Court found no motivation in the

prior art in that case; neither do I in the case at bar. In this case, which does not involve a genus patent [see discussion following], the prior art did not differentiate between the pharmaceutically acceptable salts of ODV, or possible crystalline forms.

[286] In my view, this aspect of the obvious to try test favours Pfizer.

M. The 668 Patent is not a selection patent

[287] As just noted, in my respectful view, the 668 Patent is not a selection patent. This was another point on which the parties divided. The definition of a selection patent is set out by the Supreme Court in *Sanofi*:

> [1] This appeal raises questions relating to the validity of what are known as selection patents. In the context of chemical compounds, in general terms, a selection patent is one whose subject matter (compounds) is a fraction of a larger known class of compounds which was the subject matter of a prior patent.
>
> …
>
> [9] The locus classicus describing selection patents is the decision of Maugham J. in *In re I. G. Farbenindustrie A. G.'s Patents* (1930), 47 R.P.C. 289 (Ch. D.). At p. 321, he explained that in the field of chemical patents (which would of course include pharmaceutical compounds), there are often two "sharply divided classes." The first class of patents, which he called originating patents, are based on an originating invention, namely, the discovery of a new reaction or a new compound. The second class comprises patents based on a selection of compounds from those described in general terms and claimed in the originating patent. Maugham J. cautioned that the selected compounds cannot have been made before, or the selection patent "would fail for want of novelty." But if the selected compound is "novel" and "possess[es] a special property of an unexpected character", the required "inventive" step would be satisfied (p. 321). At p. 322, Maugham J. stated that a selection patent "does not in its nature differ from any other patent."

> …
>
> [11] Although much has been written about selection patents since *I. G. Farbenindustrie*, Maugham J.'s analysis is consistently referred to and is well accepted. I find it is a useful starting point for the analysis to be conducted in this case.

[288] The issue of selection patent is not an independent basis to attack a patent; selection patents are treated like other patents in accordance with the *Patent Act* and applicable law. Issues arising out of a selection patent are considered in the obvious analysis. It is an error of law to rely on the conditions for a valid selection patent as constituting an independent basis upon which to attack the validity of a patent: *Eli Lilly v Novopharm*, 2010 FCA 197 at para 4.

[289] In the case at bar, Teva relies on the US 186 Patent and WO 851 to describe the first, or originating class of compounds disclosed, as discussed in the extract from *Sanofi* just cited.

[290] The difficulty with this argument is that while US 186 and WO 851 disclose ODV as a free base and a fumarate salt, and refer both the ODV succinate salt and the possibility of other salts, nothing in the prior art discloses the crystalline form of ODV succinate known as Form I which is the subject of each of the asserted claims 8, 9, 33, 43 and 44. While the salt was disclosed, the crystal form was not.

[291] In my respectful view one cannot have a selection patent unless the compound claimed as the selection patent is a compound that was previously claimed, *i.e.*, included within the genus of a previous patent. The second invention must be a selection from the prior art genus. The novel crystal Form I ODV succinate is a new composition of matter; it is a three-dimensional

arrangement of the atoms and molecules of ODV succinate. It was not found in the genus of any other patent. Therefore this is not a case of a second invention being selected from the prior art genus. Therefore this is not a selection patent.

[292] No previous patent claimed this crystalline form. Further, the Skilled Persons could not have predicted that this new crystalline Form I ODV succinate could or would occur. There is no evidence that the crystalline Form I ODV succinate was claimed in a prior patent or disclosed in the prior art. Because the crystal Form I ODV succinate is not a narrow class of compound covered by a previous genus, or originating patent, the crystal Form I falls outside the very nature of a selection patent by its definition: *Pfizer v Ranbaxy*, 2008 FCA 108 at para 45.

[293] I agree that the new crystal form claimed is at the heart of the invention of Claims 8 and 9 of the 668 Patent. Its use to treat depression is covered by Claim 33 which paves the way for sustained release oral formulations that could deliver identified therapeutic concentrations of ODV to the bloodstream over a prolonged period of time and reduce the overall incidence of certain side effects associated with higher peak blood concentrations. It is this formulation that is the invention in Claims 43 and 44 of the 668 Patent.

N. <u>What is the course of conduct followed which culminated in making the invention?</u>

[294] The course of conduct in this specific case, that is, the invention story regarding the 668 Patent is outlined above as deposed by Drs. Shah and Park. Based on my findings in that regard, I am unable to conclude that the course of conduct that was followed and which culminated in the crystalline Form I ODV succinate was routine.

[295] I accept Teva's submission that the salt form ODV succinate was made as a new composition of matter - [redacted] However, and while much was made of it and without doubting its relevance on this branch of the *Sanofi* inquiry, the time taken to make a new invention is but a single factor. This is particularly the case given the evidence that this particular salt and crystalline form was not identified or predicted or predictable. I have noted the evidence, and already found that salt forms in fact were seen as counter-intuitive [redacted] based on the fact that the salt form ODV fumarate had not worked.

[296] [redacted]

[297] Moreover, the invention story in this case did not start at the salt screen or the identification of the succinate salt as a possible candidate for further testing and drug development. To start the analysis there is to ignore the work done before the most recent salt screen began, including work on the fumarate salt, and the work done developing an ultimately unsuccessful pro-drug. And one may not ignore the very considerable work in terms of the *in vitro* and *in vivo* and human testing that Wyeth performed after the detailed and salt screening and specialized crystal polymorph screening.

[298] [redacted] But again that was neither predictable nor predicted. Moreover, additional testing was needed to determine whether there were other forms of ODV succinate, and very importantly, additional experimentation was required to determine which if any crystal form of ODV succinate was the most stable, *i.e.*, the best candidate for further drug development. The fact that Wyeth also discovered what turned out to be the most stable crystal form of Form I ODV succinate and did so before Wyeth engaged SSCI does not detract from the fact the salt and crystal experimentation required was much more than routine.

[299] This confirms my earlier finding that the Skilled Person looking at the prior art and common general knowledge would see a research program in terms of finding a compound suitable for drug development that had the necessary properties including solid state stability at ambient temperatures and relative humidity, solubility, permeability and bioavailability.

[300] [redacted]

[redacted]

[301] On balance, and in my respectful view, the actual course of conduct in this case entailed more than routine experimentation. It was in fact a research program. Significantly, the Skilled Person, in my view, would have foreseen it as such. The SSCI research took five months, as an example.

[302] That said, while I agree that some of the work done by Wyeth and SSCI was not arduous, viewed overall it was nonetheless difficult. In my view, in this connection, the comments of Gauthier JA in *Plavix 2* are relevant: "137... [H]owever, Rothstein J. made it clear in Sanofi that whether the separation or resolution of the enantiomers was routine or involved arduous work would assume small significance in this case when one considers the whole course of conduct that led to the decision to separate (See *Sanofi* at para 89)."

[303] These circumstances favour Pfizer in the obvious to try analysis.

i. Conclusions on obvious to try regarding Claims 8 and 9

[304] In summary, based on the above, I find on a balance of probabilities that it was not more or less self-evident to the Skilled Person that what is being tried, *i.e.*, the inventive concept or solution taught by the 668 Patent namely the crystal Form I ODV succinate as claimed in Claims 8 and 9, ought to work.

ii. Conclusions on obvious to try regarding Claims 33, 43 and 44

[305] Because Claims 33, 43 and 44 depend on Claims 8 and 9, I conclude that their respective inventive concepts, the solutions they teach, were also not obvious to try.

O. Consideration of guidance of obvious to try analysis set out in Sanofi

[306] I have made these findings without specific reference to the guidance set out at the commencement of the Supreme Court's discussion of obvious to try in *Sanofi*. There, the Court stated that the obvious to try doctrine must be "approached cautiously", that it is "only one factor to assist in the obviousness inquiry", and that obvious to try "not a panacea" at para 64.

[307] The need to be cautious approach leads me to the same conclusion as just made, as does being guided by the warning that obvious to try is not a 'panacea'.

[308] I turn to the Supreme Court's considerations respecting the purposes of the *Patent Act*, namely that: "[T]he patent system is intended to provide an economic encouragement for research and development. It is well known that this is particularly important in the field of pharmaceuticals and biotechnology" [at para 64]. These guiding principles confirm my finding on a balance of probabilities, that Teva's allegation of obvious to try are not justified.

[309] In summary, the guidance provided by the Supreme Court with respect to obvious to try supports the conclusions drawn.

P. Conclusion on obviousness

[310] In my respectful view, the Applicant has established on a balance of convenience that Teva's allegation of obviousness is not justified.

4. Utility

[311] Utility is required for an invention to be patentable: *Patent Act* at s 2:

invention means any new and useful art, process, machine, manufacture or composition of matter, or any new and useful improvement in any art, process, machine, manufacture or composition of matter; *(invention)* [Emphasis added.]	***invention*** Toute réalisation, tout procédé, toute machine, fabrication ou composition de matières, ainsi que tout perfectionnement de l'un d'eux, présentant le caractère de la nouveauté et de l'utilité. *(invention)* [Soulignement ajouté.]

[312] Previously, the discussion of utility would start with identifying the need for utility to be either demonstrated or soundly predicted, and then discuss the Promise Doctrine. However, subsequent to the hearing in this matter, the Supreme Court of Canada held that "the application of the Promise Doctrine is not the correct approach to determine whether a patent has sufficient utility." See *AstraZeneca v Apotex*, 2017 SCC 36 [*AstroZeneca*] at para 2. I invited submissions from the parties concerning *AstraZeneca* and the case at bar. Both parties filed main and responding submissions.

[313] Teva properly conceded that in view of *AstraZeneca*, "it is clear that the 'promises' of the 668 Patent are no longer 'the yardstick against which utility is measured'." Instead, Teva

submitted that: "it is clear that the mischief of overpromising is addressed instead by reference to s 27(3) and s 53 of the *Patent Act*, and that a disclosure which is not correct and full, or which states an unsubstantiated use or operation of the invention, may be found to fail to fulfill the requirements of s 27(3)."

[314] In this connection, I note Teva did not refer to subsection 27(3) in its memorandum of fact and law, nor did Teva refer to subsection 27(3) in the outlines of argument filed at the hearing. While Teva originally alleged misrepresentation contrary to s 53 of the *Patent Act*, it withdrew that allegation at the hearing.

[315] Teva submitted argument on two main points arising out of *AstraZeneca*, obviousness and insufficiency:

> Teva's Notice of Allegation addressed the same factual allegations regarding the deficiencies of the data underlying the 668 Patent under various headings, including obviousness, utility and insufficiency of disclosure. In view of *Esomeprazole*, the deficiencies of the data underlying the 668 Patent are properly addressed in relation to obviousness (there is no special advantage) and insufficiency (the disclosure of the properties of the salts of ODV is not correct and full). The evidence shows that the 668 Patent is invalid for both obviousness and insufficiency.

[316] While I agree that Teva's NOA addressed deficiencies in data underlying the 668 Patent, the NOA did so only in the context of its allegation that the 668 Patent is a selection patent, identifying this allegations under the combined heading "INSUFFICIENCY / INVALID SELECTION."

[317] In terms of obviousness, Teva repeated the arguments it made throughout that the results of salt screens have in other cases been found to be obvious "as addressed in detail in Teva's previous submissions", adding that "[A] scintilla of utility does not render a salt non-obviousness: the utility of table salt does not make table salt patentable." On the evidence in this case, however, I have found that the invention of the crystalline Form I ODV succinate was neither obvious nor obvious to try.

[318] With respect to insufficiency, Teva notes that *AstraZeneca* held, among other things, that a "disclosure which is not correct and full, or states an unsubstantiated use or operation of the invention, may be found to fail to fulfill the requirements of s. 27(3)." However, as noted, Teva did not refer to subsection 27(3) in its memorandum of fact and law, or for that matter, in any of the outlines filed at the hearing.

[319] Teva noted *AstraZeneca*'s acceptance that "inventions are like a many-faceted prism: multiple claims (sometimes running into the hundreds) covering all facets are allowed in the same patent if a 'single general inventive concept' links them."

[320] Teva argued that the 668 Patent is a selection patent that is primarily based upon the properties of the succinate salt of ODV such that the single general inventive concept was ODV succinate, the same inventive concept as Claim 1. It argued that the "disclosure of the 668 Patent is insufficient, as the advantages stated in the 668 Patent cannot meet the requirements for a valid selection patent." In this respect, Teva relied on *Eli Lilly v Novopharm*, 2007 FC 596 at where Justice Hughes stated:

> The general jurisprudence as to sufficiency of disclosure must be considered in light of the particular requirements respecting selection patents [*i.e.*] that the inventive feature of selection of a compound or group of compounds from a larger group must reside in the unexpected or surprising attributes of the selected compound or groups and that this inventive feature must be clearly set out in the specification.

[321] I have previously found that the 668 Patent is not a selection patent. Therefore, and in my respectful view, Teva's arguments based as they are on the incorrect premise that the 668 Patent is a selection patent, are not relevant to the inutility analysis post-*AstraZeneca*.

[322] Pfizer in its post-hearing *AstraZeneca* filing submitted that in *Astrazeneca*, the Supreme Court "introduced a new two-step utility approach. First, courts must identify the subject matter of the invention as claimed in the patent. Second, courts must consider whether that subject matter is useful. A 'scintilla of utility will do,' and a single use is sufficient to satisfy the utility requirement under section 2 of the *Patent Act* … even where multiple uses are disclosed or described." Pfizer added:

> 2. While the 668 Patent may disclose multiple uses relating to the various aspects of its subject matter, the subject matter of claims 8 and 9 is the novel crystal form - Form I ODV succinate. Applying the Supreme Court's guidance, the utility associated with that novel crystal form is solid-state stability. The inventors demonstrated the solid-state stability of the crystal form prior to the relevant date. This is a complete answer to Teva's allegation that the subject matter of claims 8 and 9 was not "useful" under section 2 of the *Act*.
>
> 3. Teva cannot reasonably maintain its position that these claims lack utility in light of the decision in *AstraZeneca*. It has not contested that the stability of Form I ODV succinate was demonstrated. Rather, its argument that the Asserted Claims lacked utility was based on its allegation that claims 8 and 9 were associated with multiple, overarching promises, including promises

> relating to the comparative properties of the salt and the reduction of side effects.

[323] In this connection the Supreme Court in AstraZeneca itself sets out the correct approach to utility:

> (2) The Correct Approach to Utility
>
> [52] The words in s. 2 of the Act ground the type of utility that is pertinent by requiring that it is the *subject-matter* of an invention or improvement thereof that must be useful. For the subject-matter to function as an inventive solution to a practical problem, the invention must be capable of an actual relevant use and not be devoid of utility. As stated by Justice Binnie in *AZT*, a patent "is a method by which inventive solutions to practical problems are coaxed into the public domain by the promise of a limited monopoly for a limited time" (para. 37, (Emphasis added)).
>
> [53] Utility will differ based on the subject-matter of the invention as identified by claims construction. Thus, the scope of potentially acceptable uses to meet the s.2 requirement is limited - not *any* use will do. By requiring the usefulness of the proposed invention to be related to the nature of the subject-matter, a proposed invention cannot be saved by an entirely unrelated use. It is not sufficient for a patentee seeking a patent for a machine to assert it is useful as a paperweight.
>
> [54] To determine whether a patent discloses an invention with sufficient utility under s.2, courts should undertake the following analysis. First, courts must identify the subject-matter of the invention as claimed in the patent. Second, courts must ask whether that subject-matter is useful - is it capable of a practical purpose (*i.e.* an actual result)?
>
> [55] The Act does not prescribe the degree or quantum of usefulness required, or that every potential use be realized - a scintilla of utility will do. A single use related to the nature of the subject-matter is sufficient, and the utility must be established by either demonstration or sound prediction as of the filing date (*AZT*, at para. 56).

[324] The first question is to identify the subject-matter of the invention as claimed in the patent. The second question the Court must ask is whether that subject-matter is useful - is it capable of a practical purpose (*i.e.* an actual result). The utility must be either demonstrated or soundly predicted. Only a scintilla of utility is required.

A. First identify the subject-matter of the invention as claimed in the patent, and second, is that subject-matter useful – is it capable of a practical purpose (i.e. an actual result)

[325] *AstraZeneca* states at para 53 that "utility will differ based on the subject-matter of the invention as identified by claims construction." Utility is assessed on a claim by claim basis after *AstraZeneca* as it was before *AstraZeneca*: *AstraZeneca v Apotex*, 2015 FCA 158, paras 4 and 5, and *Apotex v Pfizer*, 2014 FCA 250, in accordance with s 58 of the *Patent Act* and para 46 of *AstraZeneca* itself.

[326] Therefore the utility analysis will proceed on a claim by claim basis, and having regard to the construction given each of the asserted claims in the 668 Patent, namely Claims 8, 9, 33, 43 and 44. It should be recalled that the parties substantially agreed on the construction of Claims 8, 9 and 33.

[327] **Claims 8 and 9 -** The parties agreed that the subject matter of Claims 8 and 9 is Form I ODV succinate. The subject matter of claims 8 and 9 is the novel crystalline form of ODV succinate, which is Form I ODV succinate. This answers the subject matter of the invention and the first part of the *AstraZeneca* inquiry.

B. Is Form I ODV succinate, the subject matter of Claims 8 and 9, useful - is it capable of a practical purpose (i.e. an actual result)?

[328] Pfizer says, and I agree, that by the relevant date it was established that Form I ODV succinate was useful as a stable, solid-state form of ODV succinate. In my view, this practical usefulness is related to the subject matter of Claims 8 and 9 given the useful and important purpose in drug development to identify a solid form of a drug that is stable under relevant conditions including manufacture, distribution, and storage until administration to the patient. To the same effect was the testimony of Teva's Dr. Fiese who agreed that stability in terms of ambient conditions of relative humidity and temperature made a better candidate for a drug, *i.e.*, "it will not change on you."

[329] In this connection, I conclude that stability was demonstrated by the facts, which are not contested, namely that Form I ODV succinate was shown to be stable at ambient room temperature and up to 105^0C, and physically stable from 5% to 95% relative humidity. [redacted] These were the findings of Dr. Park at SSCI which I have accepted: see above at paras 136, 138 and 145.

[330] Pfizer also argued that the practical usefulness of the drug as a stable solid form is alone sufficient utility under *AstraZeneca* in this context. I agree. However, because they were argued before me, I will review other alleged utilities.

[331] Pfizer says that the inventors of the 668 Patent had demonstrated that ODV succinate and Form I ODV succinate had additional useful and practical properties namely, improved solubility, permeability and bioavailability over previous forms of ODV: ODV free base and fumarate. As the following analysis based on my previous findings confirms, I agree.

[332] The utility of ODV succinate the salt (Claims 1 to 7) was both demonstrated and soundly predicted. It was demonstrated by the high and improved solubility and its increased solubility across all relevant pH ranges in the GI over ODV fumarate [redacted], as set out previously in these Reasons. It had improved and high permeability as demonstrated by its increased permeability across the rat GI tract over ODV fumarate [redacted] as shown in the rat perfusion tests and resulting widely accepted predictive Peff and Fa values. Solubility was therefore demonstrated and based on a sound line of reasoning.

[333] ODV succinate also provided improved high bioavailability. Bioavailability is largely a function of solubility and permeability; improvements in both solubility and permeability will result in an improvement in bioavailability. [redacted] Predicted human oral bioavailability from the rat perfusion test was higher for succinate than for either fumarate [redacted]

[334] Moreover, in my view the ODV succinate salt's utility was also soundly predicted mostly for the same reasons, namely it having high, suitable and improved solubility, together with

improved permeability. The rat permeability calculations showed that ODV succinate would have higher overall bioavailability than fumarate [redacted], rat perfusion testing and the use of Peff and Fa values being well-accepted models of GI permeability.

[335] I should also note that Teva's arguments against the utility of Form I ODV succinate was based entirely on the Promise Doctrine which has now been rejected; previously, Teva did not dispute that Form I ODV succinate had utility outside the Promise Doctrine.

[336] **Claims 33, 43 and 44 -** The other asserted Claims relate to additional subject matter disclosed by the 668 Patent. Specifically, and as I found as a matter of claims construction, and as it depends on claims 8 or 9, Claim 33 relates to the use of Form I ODV succinate in the treatment of depression.

[337] Claim 44, as it depends on Claims 8 or 9, and as I have found as a matter of claims construction, relates to the use of a sustained release formulation of Form I ODV succinate to induce a particular blood plasma concentration and reduce the incidence of side effects that occur with a non-sustained release formulation. Claim 44 relates to the same sustained release formulation containing ODV succinate in any form.

[338] These claims cover further uses of the subject matter of Claims 8 and 9, which brings us the next question per *AstraZeneca*: whether that subject-matter is useful - is it capable of a practical purpose (*i.e.* an actual result).

C. Are the subject matters of Claims 33, 43 and 44 useful – are they capable of a practical purpose (i.e. an actual result)?

[339] **Claim 33 -** In my respectful view, the inventors had both demonstrated and soundly predicted that Form I ODV succinate was capable of a practical purpose (*i.e.* an actual result) namely, that it could be used in the treatment of depression.

[340] In my view, the inventors demonstrated and, in the alternative, soundly predicted that Form I ODV succinate could be used in the treatment of depression. ODV itself was already known in the art to be useful for the treatment of depression, so long as it could be effectively administered. The Skilled Person would know that if any particular form of ODV succinate could be effectively administered into a patient's bloodstream, it would similarly be useful for this purpose because ODV would have dissociated. The inventors of the 668 Patent had demonstrated by the filing date that Form I ODV succinate could be administered so as to result in effective blood concentrations of ODV in human patients. Thus, any utility associated with Claim 33 was also demonstrated.

[341] In my view Form I ODV succinate' utility to treat depression was also soundly predicted based on the known pharmacology of ODV and the fact that Form I ODV succinate had been shown to be capable of getting into the bloodstream. It was known that ODV was pharmacologically active as a SNRI and that ODV was the active metabolite of venlafaxine, which was approved and used for the treatment of depression as EFFEXOR and EFFEXOR XR. In other words, the anti-depression pharmacological activity of ODV was known. Further, just as noted Form I ODV succinate was shown to be capable of getting into the bloodstream at

therapeutically effective concentrations. In my view, the conclusion that Form I ODV succinate could get into the bloodstream where it would be expected to be useful for all of the clinical uses for which ODV was already known to be useful including usefulness to treat depression was therefore based on a sound line of reasoning.

[342] **Claims 43 and 44**. - In my view the inventors demonstrated at the relevant time that sustained release formulations of ODV succinate (specifically, Form I) that induced the requisite blood plasma level led to an overall reduction in side effects as compared with immediate release formulations, as explained by Dr. Polli: "…sustained release formulations which resulted in peak plasma concentrations of less than 225 ng/mL (the lower end of the range for the immediate release formulation) would result in a reduction of these side effects over immediate release formulations of ODV succinate."

[343] These formulations are intended to release a drug more slowly in order to reduce blood concentrations and therefore side effects.

[344] Pfizer notes that the issue of side effects is irrelevant insofar as Claims 8, 9 and 33 are concerned.

[345] For Claims 43 and 44 in terms of the utility inquiry after *AstraZeneca*, the issue is whether, as *AstraZeneca* teaches, the subject matter of these claims - which is a sustained release formulation of ODV succinate that results in a Cmax of less than 225 ng/mL - is useful. In my respectful view, the usefulness of the sustained release formulations in reducing side effects

compared to immediate release was demonstrated by the inventors and reported in the 668 Patent, as just discussed, and confirmed by Dr. Shah and Dr. Polli and as stated in the 668 Patent.

[346] This usefulness is clearly a practical purpose (*i.e.* an actual result). Therefore Pfizer has met the requirements of the *Patent Act*'s usefulness requirements as determined in *AstraZeneca*; additional statements in the 668 Patents referring to a reduction of side effects need not be considered because they are irrelevant.

[347] Given the above, I am satisfied on a balance of probabilities that Teva's allegations of inutility are not justified.

VIII. Conclusion

[348] Having concluded on a balance of probabilities that Pfizer has established that Teva's allegations of obviousness and lack of utility are not justified, the Applicant Pfizer is entitled to an order prohibiting the Minister of Health from issuing a Notice of Compliance in respect of a Notice of Allegation sent by Teva Canada Ltd. to Pfizer Canada Inc., previously Wyeth LLC, dated July 10, 2015, in respect of Canadian Patent No. 2,436,668 which is issued as part of the Judgment herein.

IX. Costs

[349] Costs shall follow the event and Pfizer shall have its costs against Teva as set out in the terms, which the Pfizer and Teva agreed upon in advance of these reasons, and which are scheduled to this Judgment.

X. Confidential Reasons

[350] These reasons contain information subject to a Protective Order and are therefore marked Confidential. The Parties shall have 20 days to consult with one another and advise the Court what if any portions they wish redacted, failing which these reasons will become the public reasons and be placed on the public file.

JUDGMENT

THIS COURT'S JUDGMENT is that:

1. The application is granted.
2. The Minister of Health is prohibited from issuing a Notice of Compliance in respect of a Notice of Allegation sent by Teva Canada Ltd. to Pfizer Canada Inc., previously Wyeth LLC, dated July 10, 2015, in respect of Canadian Patent No. 2,436,668.
3. Teva shall pay Pfizer its costs of this application as per Schedule "A", Agreed Terms of Costs Order attached hereto, Paragraph 2 having been deleted as not applicable given the result.
4. The Parties shall have 20 days to consult with one another and advise the Court what if any portions of this Confidential Judgment and Reasons they wish redacted, failing which these reasons will become the public reasons and placed on the public file accordingly.

"Henry S. Brown"
Judge

Schedule "A"

Agreed Terms of Costs Order

1. The successful party will be awarded costs in accordance with the following directions, provided that the following directions in no way modify or supersede any existing Orders or Directions with respect to costs for particular motions or steps before the hearing of this Application:
    a. Costs are to be assessed at the middle of Column IV of Tariff B;
    b. No costs are recoverable for in-house counsel, law clerks, students and support staff;
    c. Costs are recoverable only for those experts who provided affidavits or reports that were filed in the proceedings (the "allowable experts");
    d. The hourly rate for allowable experts shall not exceed the hourly rate of senior counsel;
    e. Fees paid to allowable experts for time not spent preparing the expert's own affidavit/report or preparing for the expert's own cross-examination are recoverable only where it is demonstrated that it was reasonable and necessary to provide technical assistance to counsel;
    f. Counsel fees shall be assessed on the basis of:
        i. one senior and one junior counsel at the hearing;
        ii. one senior and one junior counsel in conducting cross-examinations; and
        iii. one senior counsel in defending cross-examinations;
    g. Travel and accommodation expenses will be assessed on the basis of economy air fares and single rooms; and

h. Photocopying costs will be assessed at $0.25 per page, and the number of recoverable copies shall be limited to that which is reasonable and necessary.

FEDERAL COURT

SOLICITORS OF RECORD

DOCKET:	T-1399-15
STYLE OF CAUSE:	PFIZER CANADA INC. AND WHETH LLC v TEVA CANADA LIMITED AND THE MINISTER OF HEALTH
PLACE OF HEARING:	TORONTO, ONTARIO
DATE OF HEARING:	APRIL 3, 2017
ORIGINAL AND CORRECTED CONFIDENTIAL JUDGMENT AND REASONS:	BROWN J.
DATED:	AUGUST 22, 2017
PUBLIC JUDGMENT AND REASONS:	BROWN J.
DATED:	SEPTEMBER 22, 2017.

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