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Ottawa, Ontario, September 22, 2017

PRESENT: The Honourable Mr. Justice Brown

BETWEEN:

PFIZER CANADA INC. and WYETH LLC

Applicants

and

APOTEX INC. 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 Apotex Inc., [Apotex] to Pfizer Canada Inc., previously Wyeth LLC [Pfizer or Wyeth], dated January 21, 2016, 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] At issue are claims 8, 9, 33, 43 and 44. While Apotex advanced other grounds in its NOA and memorandum, some were subsequently abandoned such that now Apotex alleges the 668 Patent is invalid on the grounds of obviousness, inutility, non-infringement, anticipation and double patenting.

II. Procedural Note

[3] As a procedural note, this case was argued after I heard argument in *Pfizer Canada Inc and Wyeth LLC v Teva Canada Limited and The Minister of Health*, in respect of which I delivered reasons and judgment in 2017 FC 777. These two cases involve different NOAs filed by different second persons, against the same first persons in respect of the same 688 Patent. While the invention story in both is essentially the same, the grounds of alleged 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.

[4] As guidance for those reading both decisions, while obviousness and inutility are at issue in both decisions, Apotex also advanced allegations of non-infringement, anticipation and double patenting which Teva did not advance in its proceeding. Claims construction is contested in this proceeding, but Claims 8 and 9 were agreed upon in the Teva proceeding. Apotex also raised overpromising in this proceeding as a ground of invalidity arising out of subsection 27(3), which Teva did not advance in its proceeding.

III. Summary of Conclusions

[5] In the reasons that follow, I find on a balance of probabilities that Apotex's allegations of invalidity due to obviousness, inutility, anticipation, and double patenting, together with Apotex's allegation of non-infringement are not justified. I find no merit in the arguments of invalidity based on "overpromising" contrary to subsection 27(3) of the *Patent Act*. Therefore, Pfizer will have its Order of prohibition, together with costs on terms the parties agreed on and which are set out in these Reasons.

IV. Witnesses

[6] The parties in their pre-hearing filing provided the following information on the witnesses, to which I have added minimally:

Pfizer's fact witnesses:

Dr. Syed Shah: 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 1990s 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.

Dr. Aeri Park: A former Principal at SSCI Inc., the research laboratory hired by Wyeth to conduct polymorph 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. Dr. Park is a named inventor on the 668 Patent.

Pfizer's expert witnesses:

Dr. Syed Shah: 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 1990s 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.

Dr. James Polli: 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 has experience in the fields of pharmaceutics, pharmacokinetics and bioavailability.

Dr. Pierre Blier, MD: Pierre Blier is a full professor in the Departments of Psychiatry and Cellular and Molecular Medicine at the University of Ottawa in Ontario, Canada. He also serves as the Director of the Mood Disorders Research Program at the

University of Ottawa Institute of Mental Health Research at the Royal Ottawa Hospital. He has experience in the fields of neuropharmacology and psychiatry.

Dr. Jerry Atwood: Jerry Atwood is Chairman of the Department of Chemistry and Curators' Professor at the University of Missouri-Colombia. He has research and academic experience in the fields of supramolecular chemistry, solid-state chemistry, crystal growth, crystal engineering, materials testing, X-ray crystallography, organic chemistry, pharmaceutical chemistry, inorganic chemistry and polymer chemistry.

Dr. Allen Myerson: Allan Myerson is a Professor of the Practice of Chemical Engineering at the Massachusetts Institute of Technology ("MIT"). He has research and academic experience in industrial crystallization and the crystallization of pharmaceutical solids.

Apotex's expert witnesses:

Dr. Alan Parr, Ph.D.: Dr. Alan Parr is an independent consultant on matters related to the biopharmaceutics of pharmaceuticals. He has approximately 30 years of experience working in the pharmaceutical industry, including with Glaxo and its successor companies Glaxo Wellcome and GlaxoSmithKline. Dr. Parr has experience in the *in vivo* evaluation of dosage forms, biopharmaceutics, pharmacokinetics, drug absorption and bioavailability/bioequivalence testing.

Richard J. Bastin: Richard J. Bastin is the Director of RJB Pharma Consulting Ltd., a consultancy business that offers advice, support and training on drug developability, process development, product development and Chemistry Manufacturing Controls strategy to pharmaceutical and biotechnology companies.

Jonathan Steed, Ph. D.: Jonathan Steed is a Professor of Chemistry at Durham University in the United Kingdom. His research focusses on crystallography, crystallization, solid state chemistry, coordination chemistry and intermolecular interactions in solids.

V. Facts

1. Background

[7] The 668 Patent concerns a drug called o-desmethyl-venlafaxine, henceforth referred to as ODV. ODV is a serotonin and norepinephrine reuptake inhibitor [SNRI] used 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. Pfizer argues and as will be seen, I have accepted that 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.

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

[9] It is common ground that ODV itself and its use to treat depression have been known for some time. Venlafaxine - which metabolizes into ODV - was previously patented and approved to treat depression. Wyeth had ODV in hand since at least 1990. Wyeth and Pfizer have 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 or sustained release version of venlafaxine (which also converts in the body to ODV but at a slower rate). ODV is the API in both EFFEXOR and EFFEXOR XR.

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

[11] ODV and "pharmaceutically acceptable salt forms thereof" were known and are claimed in both claim 22 in US Patent No. 4,535,186 (US 186), issued in 1985, and in claim 21 of Canadian Patent No. 1,248,540 (CA 540), issued to a Pfizer predecessor company in 1989.

[12] "Pharmaceutically acceptable salts" as the term is used in US 186 and CA 540 are formed by reacting an acid together with and a base. ODV is a base; therefore, to make a salt an appropriate acid is required for such reaction. Both US 186 and CA 540 claim ODV succinate as one of 11 "illustrative" pharmaceutically acceptable salts, and therefore include a reference to reacting ODV with succinic acid.

[13] However, there is no suggestion in either US 186 and CA 540, or elsewhere in the prior art, that the salt ODV succinate had ever been made before. Likewise there is no suggestion that any crystalline form of the salt ODV succinate had ever been known or made before. Further, there is no evidence or argument that the crystal Form I ODV succinate, which Wyeth alleges is

the inventive concept of Claims 8 and 9, had ever been known or made before it was made by Wyeth.

[14] In addition to disclosure in the Canadian (CA 540) and American (US 186) patents just referred to, it is 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. Once again however there is no suggestion that ODV succinate had ever been made, or that the crystalline ODV succinate had ever been made, or that Form I ODV succinate had ever been made before it was created in Wyeth's laboratories.

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

[16] As is also well known, depression is a serious medical condition that can be and is often debilitating. 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.

2. The Invention Story

[17] The essence of the inventive story is 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 to the dispute over the alleged lack of utility and in other respects as well. In my view the inventive story warrants being set out in some detail; I will summarize it first.

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

[19] 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 they describe. I appreciate they are both named inventors on the 668 Patent, but am not in any way persuaded that this affected their evidence whether deposed to in their affidavits, or in cross-examination.

[20] Wyeth, now Pfizer, had venlafaxine as one of its drugs. As such, it knew that ODV was the active metabolite of venlafaxine. Pfizer at first through a predecessor company and then in its own name marketed venlafaxine as EFFEXOR and EFFEXOR XR. EFFEXOR delivered venlafaxine immediately, but for many patients that meant 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 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 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.

[21] 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 to be metabolized or converted into ODV, which then acted as the anti-depressant in the brain.

[22] The new ODV drug that 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 the oral dose sought, involves permeating the gastrointestinal [GI] tract.

[23] The searched-for new ODV drug had to be a stable, that is, 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.

[24] The ODV drug form Wyeth was searching for had to be able to dissolve in the gastrointestinal [GI] tract *i.e.*, it had to be 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.

[25] 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.

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

[27] Wyeth and SSCI eventually identified a solid crystalline form of ODV that was stable, soluble, permeable 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 before made or disclosed until it was created by Wyeth. I should note that Apotex raises invalidity based on anticipation therefore newness is in issue, and will be dealt with later in these Reasons.

[28] 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 it would have been impossible for the Skilled Person to know or 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, let alone Form I ODV succinate would be in terms of stability, solubility, permeability, bioavailability and adverse effects; none of this would be known without doing empirical research. 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.

[29] 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, and because the work done by SSCI entailed a different type of screening, known as polymorph or crystal screening. Pfizer and Apotex 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).

[30] Wyeth not only created the ODV succinate salt, but went further and discovered and created a crystalline form of that salt which has become known as the crystalline Form I ODV succinate. Wyeth however did not know that the crystal it created [redacted] Wyeth with its subcontractor SSCI went further.

SSCI found another three crystalline and one amorphous forms of ODV succinate in addition to crystalline Form I ODV succinate created by Wyeth and relied upon by Pfizer in Claims 8 and 9 of the 668 Patent.

[31] [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.

3. Invention Story in more detail: the evidence of Pfizer's Dr. Shah

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

[33] 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]

[34] Wyeth was also interested in two further matters: 1) improving patient compliance, that is, improving the chances of patients actually taking their medication as prescribed, and 2) the need to develop a new drug with reduced 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.

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

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

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

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

[39] 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, a point Apotex challenged and which I will address shortly. 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 this new 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.

[40] 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.

[41] 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.

[42] The following outlines these steps in more detail.

4. Experimentation with ODV fumarate

[43] 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. ODV fumarate was known in the art at the time because it was disclosed as Example 26 of US 186 as a crystalline salt.

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

[45] 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]

[46] As indicated previously, [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 when it ceased to be in salt form ODV fumarate, in the GI tract, where it lacked suitable bioavailability, the same dissociation but poor bioavailability could obtain with the drug ODV when reacted to form other salts. In other words, if the dissociated drug ODV did not do well in terms of permeability when orally dosed as ODV fumarate, it was unclear why another salt form of ODV might behave any better:

Affidavit of Dr. Shah, para 22.

[47] Apotex argues that [redacted] To the extent Dr. Shah refers to the views of others at Wyeth, Apotex is correct. However, Dr. Shah also deposed to and certainly had personal knowledge of the fact that [redacted]

[redacted], namely that since salts that are reasonably soluble (like ODV fumarate) are usually completely dissociated by the time they get to the GI tract, it was unclear how much impact a new salt would have on improving permeability. [redacted]

5. Attempt to form pro-drug of ODV

[48] Wyeth also 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 by the body. Depending on the modifications that are made, a pro-drug may have improved solubility, dissolution or absorption over the active molecule.

[49] [redacted]

[50] [redacted] In this evidence, Dr. Shah was relying on what had been reported to him as I agree with Apotex that he had no involvement in Wyeths' ODV pro-drug development program, which it appears led to at least one successful patent application of which Dr. Shah was unaware.

[51] However, I accept Dr. Shah's main evidence on this point, namely that Wyeth conducted pro-drug development work apart from Dr. Shah's salt and crystalline drug development work in connection with ODV. While Apotex calls the Wyeth's attempt to find a pro-drug a "diversion", the fact is that both parties agree that Wyeth undertook pro-drug exploration and development work. I accept Dr. Shah's evidence that it took place: this is not disputed by Apotex's expert Dr. Steed who disparaged pro-drug development regarding ODV. Accepting Apotex's argument that Wyeth succeeded in making and even patenting a pro-drug does not establish that pro-drug development was irrational or unreasonable; in my view, it proves the opposite and justifies pro-drug development work that Apotex says would not have been done by a Skilled Person.

6. Attempt to form an acceptable salt of ODV

[52] The third option pursued by Wyeth (after the fumarate salt and pro-drug) 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.

[53] I also accept that it was known, as 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.

[54] ODV is a base. Therefore, in order to attempt to make a salt with ODV, it was necessary to interact the base, ODV, with an acceptable acid.

[55] [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.

[56] [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]

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

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

[59] After discarding the [redacted] salt as a candidate, Wyeth continued to prepare and test 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.

[60] 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]

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

[redacted]

[redacted]

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

[63] Apotex notes that ODV succinate was one of the first salts identified after Wyeth's salt screening commenced; [redacted], as reported in para 60(e) above.

7. Polymorph and crystal screening

[64] 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.

[65] [redacted]

[redacted]

[66] [redacted]

[67] 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. It is not disputed that 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).

[68] 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.

8. Solubility

[69] After identifying these crystalline salts, Wyeth next evaluated the solubility of the potential drug candidates. Solubility of a drug candidate was important. In order for an oral dose of a drug to be absorbed in the GI tract, it needed 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.

[70] In addition, Wyeth was 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.

[71] In this connection, [redacted]

[redacted] I find that the succinate salt was more soluble which made it a likely candidate for further drug development.

9. The Preparation of ODV Succinate

[72] Given this, it is not surprising and the evidence I accept is that the 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]

[73] [redacted]

[74] [redacted]

[75] [redacted]

[76] 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.

10. Permeability and bioavailability testing

[77] 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.

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

[redacted]

[79] [redacted]

[80] [redacted]

[81]

[82] However, regarding point 1, Dr. Shah testified that in another case in which White & Case, a US law firm was involved, he was told that they had tried to obtain that information and were not able to find the

[83] , Dr. Shah's reply affidavit clearly rejected Apotex's concerns, which I find were speculative to being with. Dr. Shah deposed:

4.

[84] Dr. Shah's explanation makes sense and I accept that ODV fumarate was a natural reference salt for permeability testing of novel salt forms, which included [redacted] and the rat perfusion *in vivo* tests.

12. Rat perfusion test

[85] 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.

[86] 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.

[87] The rat perfusion tests involved injecting a solution of ODV succinate directly into clamped off sections of the GI tract of living 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.

[88] [redacted]

[89] 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.

[90] 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 what is known as a "Fa" value ("fraction absorbed"), which is the percentage of the drug present reliably predicted to be absorbed in the human GI tract.

[91] 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 regions.

[92] 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).

[93] 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).

[94] 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]

[95] Apotex raises issues in connection with the rat perfusion tests (going to Apotex's inutility argument). Apotex argued that the rat perfusion tests were not demonstrative but only predictive, that the tests only showed comparable not improved absorption and were themselves unreliable, and that other Wyeth tests showed ODV free base, fumarate and succinate were all favourable which test results were not available. I accept Dr. Shah's evidence in interpreting the results over that of Dr. Bastin on the first two points, and am not persuaded that Dr. Shah was being anything but truthful in his evidence on the third. In connection with missing reports it should be recalled that [redacted], all of which were exhibited to Dr. Shah's affidavit.

13. Beagle dog testing

[96] 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 previously 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."

[97] Thus ODV succinate was advanced to *in vivo* beagle dog tests. However, the fumarate salt was not subject to beagle dog testing because Wyeth had already established that ODV fumarate had poor bioavailability.

[98] In the beagle dog testing, Dr. Shah's evidence, which I accept, was that Wyeth was looking for an oral dosage form 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.

[99] 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.

[100] 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.

[101] [redacted]

[102] 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.

14. Human testing

[103] With the [redacted] in vivo testing in rats and beagle dogs showing positive results, Wyeth moved to testing in with 18 human volunteers.

[104] 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.

[105] 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 immediate and sustained release 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]

[106] The results of the human studies are summarized in [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.

[107] 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 surmised 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.

[108] 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]

[109] 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.

[110] 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 immediate release 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. Thus I reject Apotex's argument that this concentration is "arbitrary".

[111] 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 versions of ODV succinate when in fact

there was one report for each: this error is not material to the improvement in side effects of the sustained release version over the immediate version; as Dr. Shah deposed "it does not affect the overall conclusion that the incidence of adverse events was lower for ODV succinate sustained release than ODV succinate immediate release".

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

[112] Dr. Shah's evidence, which again I accept, was that a criterion for a viable drug form was a drug form 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.

[113] 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's 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.

16. Polymorph screening and subcontracting polymorph screening to SSCI, Inc.

[114] 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.

[115] 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]

[116] [redacted]

[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.

[117] 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]

[118] 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 which Wyeth gave to SSCI for its work.

[119] [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.

17. Dr. Aeri Park at SSCI

[120] 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.

[121] 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 specialized SSCI 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.

[122] [redacted]

[123] [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.

[124] Dr. Park's experience-based evidence 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 crystal and 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 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.</u>
>
> 22. At regular intervals throughout the screening project, I would discuss the experimental results to date with the members of my team, and <u>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.</u>
>
> [Emphasis added.]

[125] Dr. Park further deposed:

> **Generating Solid Samples**
>
> 34. 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.
>
> 35. 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]
>
> 36. The creation and analysis of new solid forms was not a rote process. It was not possible for us to predict at the outset how many solid forms we would be able to identify, what they would be, or what solid forms would result from any particular method or set of conditions. Therefore, this process often required numerous experiments and analyses, and strategy and judgment had to be employed in order to make decisions about how to proceed based on the results that we obtained.
>
> [Emphasis added.]

[126] In the process of creating and identifying new solid state forms, Dr. Park and SSCI conducted numerous other studies and experiments, as outlined below:

Characterization of Initial Solid Samples

42. [redacted]

43. [redacted]

44. [redacted]

45. [redacted]

[redacted]

46. [redacted]

47. [redacted]

48 [redacted]

49. [redacted]

50. [redacted]

51. [redacted]

Other Techniques for Analysis and Characterization

52. [redacted]

53. [redacted]

[Emphasis added.]

[127] [redacted]

[128] [redacted]

[redacted]

19. Melting points and differential scanning calorimetry (DSC)

[129] [redacted], 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.

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

20. Further temperature studies and amorphous form

[131] [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]

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

[redacted]

21. Hygroscopicity testing (a test relevant to drug stability)

[133] [redacted]

[134] [redacted]

[135])

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

24. (Crystal Form “D”)

[137]

[redacted]

[138] [redacted]

[139] SSCI ultimately identified four polymorph forms of ODV succinate, namely Forms “A”, “B”, “C” and “D”. Of these Form A had already been discovered by Wyeth; Wyeth had provided Form “A” to SSCI. Therefore, SSCI succeeded in identifying three new crystalline forms of ODV succinate. SSCI also identified one new amorphous form. In all, five forms of ODV succinate were identified by SSCI, four for the first time.

[140] [redacted]

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

25. Work on other salt candidates and screens

[142] 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 [redacted]

[143] [redacted]

[redacted]

26. Miscellaneous

[144] While Apotex raised issues in connection with the invention story concerning the racemate and enantiomers of ODV succinate in its NOA and based on evidence supplied by Apotex's Drs. Bastin and Steed, it did not pursue this issue in its memorandum or at the hearing.

VI. Issues

[145] The issues remaining in this application are:

1. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Apotex's allegation of obviousness is not justified.
2. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Apotex's allegation of inutility is not justified.
3. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Apotex's allegation of non-infringement is not justified.
4. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Apotex's allegation of overpromising in relation to subsection 27(3) of the *Patent Act* is not justified.
5. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Apotex's allegation of anticipation is not justified.

6. Whether Pfizer has discharged its burden to establish on a balance of probabilities that Apotex's allegation of double patenting is not justified.

VII. Statutory provisions and burden of proof

[146] Pursuant to section 2 of the *Patent Act*, in order to be patented, an invention must be "new" and "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.]

[147] 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.

VIII. Analysis

1. Relevant Dates

[148] The relevant dates are agreed upon and are as follows.

[149] The 668 Patent was filed in Canada on February 11, 2002, claiming priority to two previous applications dated February 12, 2001 and June 13, 2001. The application was published on August 22, 2002 and the patent issued on May 26, 2009.

[150] The relevant dates for assessing obviousness for each of the asserted claims are set out in s 28.3 of the *Patent Act*. For publicly disclosed information originating from the patentee, the relevant date is February 11, 2001. For all other publicly disclosed information, the relevant date is the claim date.

[151] Pfizer asserts that it is entitled to rely on its priority applications and that the claim date is the first priority date of the 668 patent (February 12, 2001). Apotex disputes that Pfizer has established that any one of the claims at issue is entitled to a claim of priority and asserts that the claim date is therefore February 11, 2002. However, given that the prior art and common general knowledge alleged by Apotex to obviate the asserted claims pre-date both of these dates, it is not necessary to resolve this conflict.

[152] The relevant dates for assessing anticipation are as set out in s 28.2 of the *Patent Act*. For publicly disclosed information originating from the patentee, the relevant date is February 11, 2001. For all other publicly disclosed information, the relevant date is the claim date. As previously discussed, Apotex's position is that the claim date is February 11, 2002, and Pfizer's position is that the claim date is February 12, 2001. However, given that the references alleged by Apotex to be anticipatory pre-date both of these dates, the parties agree that it is not necessary to resolve this conflict.

[153] The parties agree that utility (whether demonstrated or soundly predicted) should be assessed as of the Canadian filing date, in this case February 11, 2002.

[154] It is not disputed that 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.

2. Claims Construction

[155] 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: *Gilead Sciences, Inc v Canada (Health)*, 2016 FC 856 at paras 37-38.

[156] In this connection, 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.

[157] Pfizer also notes that a patent should be read "purposively" from the perspective of a person of ordinary skill in the art to which the patent relates. Purposive construction requires the Court to consider the words of the claims in light of the whole specification. While the words of the patent govern, the Court must consider the context in which they appear. The construction should be one that is "in the interest of fairness both to the patentee and the public": *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at paras 45, 49, 52-53.

[158] The parties dispute the construction of the asserted claims, mainly in respect of Claims 8 and 9. The following is a claims chart prepared by the parties setting out each claim in issue, the claims from which they depend (for context), and the parties' positions on construction. Note that while more are outlined below, only Claims 8, 9, 33, 43 and 44 are asserted by Pfizer:

Claim No.	**Depends From**	**Claim Language**	**Pfizer's Position on Construction**	**Apotex's Position on Construction**
1.	None	A compound which is O-desmethyl-venlafaxine succinate or a mixed salt thereof.	**Not asserted**. Covers ODV succinate, or alternatively, a mixed ODV succinate salt, in any form.	Encompasses all crystalline and amorphous forms, mono and bi ODV succinate salts, as well as mixed salts of ODV succinate.
2.	Claim 1.	A compound according to claim 1 wherein the ratio of O-desmethyl-venlafaxine to succinic acid is 1:1.	**Not asserted.** Covers ODV mono succinate in any form.	Encompasses Form I (unground), Form I (ground), Forms II, III and IV, and the amorphous form.
3.	Claim 1.	A compound according to claim 1 wherein the ratio of O-desmethyl-	**Not asserted.** Covers ODV bis succinate in any	Covers bi ODV succinate in any form. Excludes Form I

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
		venlafaxine to succinic acid is 2:1.	form.	(unground), Form I (ground), and Form II, III and IV.
4.	Claim 1.	A compound according to claim 1 which is a hydrate of O-desmethyl-venlafaxine succinate.	**Not asserted.** Covers any hydrated form (*i.e.*, a form in which water is present in the crystal lattice) of ODV succinate.	Encompasses Form I (unground), Form I (ground) and Forms II and III. Form IV, and the amorphous form are excluded.
5.	Claim 1.	A compound according to claim 1 which is O-desmethyl-venlafaxine succinate monohydrate.	**Not asserted.** 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).	Encompasses Form I (unground), Form I (ground) and Form II. Forms III and IV, and the amorphous form are excluded.
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 asserted.** 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.	As it depends on claim 5, the claim encompasses Form I (unground), Form I (ground) and Form II. Forms III and IV, and the amorphous form are excluded.
8.	Claim 6, which in turn depends from claims 1,	A compound according to claim 6 which exhibits an X-	Covers Form I ODV (mono) succinate	Covers ODV succinate that satisfies the

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
	2, 4 or 5.	ray powder diffraction pattern having characteristic peaks expressed in degrees 2θ (+ 0.2° 2θ) at 10.20, 14.91, 20.56, 22.13, 23, 71, 24.60, and 25.79.	monohydrate (*i.e.*, the crystalline form of ODV succinate, which exhibits the characteristic XRPD peaks of Figure 1).	requirements of claim 6, which depends on any one of claims 1, 2, 4 or 5, and that exhibits the specific XRPD peaks set out in claim 8. Claim 8 is not a claim to Form I per se. The claim encompasses Form I (ground). Form I (unground), II, III and IV and the amorphous forms are excluded.
9.	Claim 6, which in turn depends from claims 1, 2, 4 or 5.	A compound according to claim 6 having an endotherm at about 131° C.	Covers Form I ODV (mono) succinate monohydrate (*i.e.*, the crystalline form of ODV succinate, which exhibits a characteristic endotherm at about 131°C (¬+ 2°C)).	Covers any ODV succinate that satisfies the requirements of claim 6, which depends on any one of claims 1, 2, 4 or 5, and that exhibits an endotherm of 131ºC (±1ºC). Claim 9 is not a claim to Form I per se. The XRPD pattern of claim 8 is not a requirement of claim 9 because claim 9 does not depend on claim 8.

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
				With a variance of + 1°C (Apotex's position), claim 9 (6, 5, 4, 3, 1) encompasses Form I (ground). Form I (unground), and Forms II and IV are excluded from the claim. With a variance of + 2°C (Pfizer's position), claim 9 (6, 5, 4, 2, 1) encompasses Form I (ground), and Form II. Form I (unground) and Form IV are excluded from the claim.
33.	Any one of claim 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of depression.	As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of depression.	As it depends on claims 8 or 9, covers an effective amount of the compounds of claims 8 or 9 for the treatment of depression. See above construction of claims 8 and 9. Encompasses intravenous administration because the claim is not specific any

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
				particular mode of administration.
34.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of anxiety.	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of anxiety.	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of anxiety.
35.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of panic disorder.	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of panic disorder.	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of panic disorder.
36.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of anxiety disorder.	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of anxiety disorder.	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of anxiety disorder.
37.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of post-	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of post-traumatic stress

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
		of claims 1 to 20 for the treatment of post-traumatic stress disorder.	traumatic stress disorder.	disorder.
38.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of premenstrual dysphoric disorder.	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of premenstrual dysphoric disorder.	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of premenstrual dysmorphic disorder.
39.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of a condition selected from fibromyalgia, agoraphobia, attention deficit disorder, obsessive compulsory disorder, social anxiety disorder, autism, schizophrenia, obesity, anorexia nervosa, bulimia nervosa, Gilles de la Tourette Syndrome, vasomotor flushing, cocaine and alcohol addiction, sexual dysfunction,	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of any one of the listed conditions.	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of one of the listed disorders.

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
		borderline personality disorder, chronic fatigue syndrome, urinary incontinence, pain, Shy Drager syndrome, Raynaud's syndrome, Parkinson's disease, and epilepsy.		
40.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for enhancing of cognition or for cognition impairment.	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for enhancing cognition or for cognition impairment.	Construction is the same as in claim 33, with the exception that the use is directed to enhancing of cognition or for cognition impairment.
41.	Any one of claims 1 to 20.	Use of an effective amount of O-desmethyl-venlafaxine succinate or a mixed salt thereof as claimed in any one of claims 1 to 20 for the treatment of hypothalamic amenorrhea in a depressed or non-depressed human female.	**Not asserted.** As it depends on claims 8 or 9, use of Form I ODV succinate for the treatment of hypothalamic amenorrhea in a depress or non-depressed human female.	Construction is the same as in claim 33, with the exception that the use is directed to the treatment of hypothalamic amenorrhea in a depressed or non-depressed human female.
43.	Any one of claims 1 to 20.	Use of a therapeutically effective amount of a	As it depends on claims 8 or 9, use of a sustained	As it depends on claims 8 or 9, covers the use of an

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
		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 of 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.	release oral dosage form comprising Form I ODV succinate to induce an average blood plasma level of no more than 225 ng/ml to lower the overall incidence of the specified side effects as compared to oral administration of ODV succinate not so formulated.	effective amount of ODV succinate as described in claims 8 or 9 in a sustained release dosage form to induce a blood plasma level of no more than 225 ng/ml to lower the incidence of specific side effects resulting from the oral administration of ODV succinate. The term "therapeutically effective amount" conveys that the use is for the treatment of any disorder described and claimed by the patent (see claims 33-42). The claim is not specific to the treatment of depression. Encompasses the use of any plasma level greater than 0 ng/ml to below 225 ng/ml.
44.	None.	A sustained release formulation comprising O-desmethyl-venlafaxine succinate and a pharmaceutically acceptable carrier or	A sustained release formulation comprising O-desmethyl-venlafaxine succinate (in any form, including	Covers any sustained released formulation containing ODV succinate in any form (including, mono and bi ODV succinate salts, the

Claim No.	Depends From	Claim Language	Pfizer's Position on Construction	Apotex's Position on Construction
		excipient, wherein the sustained release formulation provides peak serum levels of up to 225 ng/ml.	Form I ODV succinate) which provides average peak serum levels of up to 225 ng/ml.	amorphous form, Form I (ground), Form (unground), and Forms II, III and IV), providing peak serum levels of up to 225 ng/ml. Encompasses sustained release formulations that provide any plasma level greater than 0 ng/ml to below 225 ng/ml. The claim encompasses all types of sustained release formulations (transdermal, oral, etc.) because the claim is not specific to any particular type of sustained release formulation. The claim encompasses use of the formulation for the treatment of any disorder described and claimed by the patent (see claims 33-42). The claim is not specific to the treatment of depression.

A. Construction of Claims 8 and 9

[159] The parties differ on the proper construction of Claims 8 and 9.

[160] Pfizer's position is set out in its memorandum as follows:

1. **Claims 8 and 9 clearly cover Form I ODV succinate.** A patent is to be read "purposively" from the perspective of a person of ordinary skill in the art to which the patent relates. Purposive construction requires the Court to consider the words of the claims in light of the whole specification. While the words of the patent govern, the Court must consider the context in which they appear. The construction should be one that is "in the interest of fairness both to the patentee and the public."
2. Claims 8 and 9 clearly relate to a particular crystalline compound, Form I ODV succinate. Claim 8 covers a compound that exhibits an x-ray diffraction pattern having seven characteristic peaks. The only such form disclosed in the patent is Form I ODV (mono) succinate (the product of Example 7). Similarly, claim 9 makes reference to Form I through its characteristic DSC endotherm provided on page 8.
3. Apotex's experts argue that claims 8 and 9 are not limited to crystal Form I, but can be read to cover a potential class - any real or imagined compound that exhibits the listed XRPD peaks. This open-ended view is wrong and does not reflect an informed, purposive reading of the patent. It is also contrary to Apotex's NOA where it stated that a skilled person would "understand claims 8 and 9 to relate to Form I ODV succinate." The proper view, as reflected in the NOA, is that a skilled person reviewing the 668 Patent would readily recognize the list of peaks set out in claim 8 and the endotherm set out in claim 9 to be the characteristic data provided for crystal Form I ODV succinate. In fact, there is no evidence of any other crystal form of any compound that exhibits this characteristic data.

[161] Apotex says in its memorandum:

> 17. Claim 8: This is a claim for crystalline ODV-S (including hydrates) which exhibits the specific XRPD peaks set out in the claim. The claim does not contain any other limitations.
>
> 18. Pfizer argues that claim 8 relates exclusively to ODV-S Form I because it has the same XRPD peaks as the disclosure reports for Form I (ground). This is an impermissible approach.

When a compound is characterized by an XRPD pattern in a claim, it is improper to use the disclosure to characterize it differently.

19. Further, claim 8 includes multiple crystal forms, namely monohydrates and other hydrates, as is clear in the claims it depends upon. And the patent's "Form 1" is not characterized by the XRPD of claim 8: the patent teaches that Form I (unground) has distinct XRPD peaks.9

20. Claim 9: This is a claim for a crystalline form of ODV-S that has an endotherm at "about 131°C". "Endotherm" can be thought of as a melting point measured by differential scanning calorimetry ("DSC")."

21. Pfizer asserts that claim 9 also relates exclusively to Form I ODV-S. Once again, this is incorrect because the claim is not drawn in this manner. Further, Example 1 of the patent is described as being (unground) Form I having a melting point(s) of 122.3 and 139.6°C. This Form I is not within the scope of claim 9.

22. Pfizer criticizes Apotex's construction of claim 9 for ignoring that Apotex's product is Form I and that Apotex does not dispute that its product falls within the scope of claim 8. This criticism illegitimately considers Apotex's product in its claims construction. Further, construing claims 8 and 9 as Form I also ignores the presumption in favour of applying different meanings to different claims. Finally, claim 9 cannot define Form I because the patent's Form II also has a endotherm of about 131°C using Pfizer's definition of "about" as discussed below.

23. The skilled person would read "about" to indicate ± 1°C. Pfizer argues that "about" ought to mean ± 2°C and thus claim 9 encompasses those compounds having an endotherm falling within the range of 129-133°C. The patent does not support this definition.

24. The patent defines "about" to mean "generally within 10%" or "alternatively...within an acceptable standard error of the mean". Neither party suggests the former definition applies to claim 9. In respect of the latter, the patent does not identify the standard of error of the mean for a DSC measurement of an endotherm, nor does it include data that would allow this to be calculated. The skilled addressee would not consider a margin of error of ± 2°C to be acceptable and Pfizer's experts have not referenced any scientific literature to the contrary.13

> 25. Further, construing the term "about" to mean ± 2°C results in Form II, with its endotherm at 127°C, falling within the scope of claim 9, directly contrary to Pfizer's construction that claim 9 embraces only Form I. Pfizer denigration of this point as "technical" is actually an acknowledgment that it is correct.14 Construing a claim in a way that is consistent with the inventors' intentions is not `technical'; it is what the Supreme Court directs.
>
> 26. Pfizer retreats to an argument about the sufficiency of Apotex's NOA. Pfizer asserts that Apotex's experts' opinion that claims 8 and 9 embrace multiple compounds is contrary to the NOA's statement that the skilled person "would understand claims 8 and 9 to relate to Form I [ODV]-S." In fact, there is no contradiction.
>
> 27. The NOA does not say that the scope of claims 8 and 9 is limited to a single compound and the allegations of overbreadth and insufficiency specifically assert that claims 8 and 9 include more than a single compound.16 The NOA asserts non-infringement of claim 9 (but not claim 8), making it clear that the NOA distinguished the subject matter of the two claims. This Court has rejected arguments regarding the sufficiency of the NOA that were based on reading a single sentence of the NOA in isolation from the rest of the document."
>
> 28. In any event, Pfizer's experts addressed the scope of the claims in chief, indicating that Pfizer had fair notice of this issue. Even if it were otherwise, experts are permitted to diverge from allegations made in a Notice of Allegation, and courts are free to differ from either or both parties on issues of construction.

[162] In my view, Claims 8 and 9 cover the crystalline Form I ODV succinate. I accept that both Claims 8 and 9 clearly relate to a particular crystalline compound, Form I ODV succinate. Claim 8 covers a compound that exhibits an x-ray diffraction pattern [XRPD] having seven characteristic peaks. The only such form disclosed in the 668 Patent is the crystalline Form I ODV (mono) succinate (the product of Example 7). Similarly, Claim 9 makes reference to Form I through its characteristic DSC endotherm provided on page 8 of the 668 Patent.

[163] The identifier XRPD set out in Claim 8 refers to Form I ODV succinate; there is no other "form" that could have that XRPD data and fall within the claim. I find that this construction gives effect to the intention of the inventor and does so in the context of the patent as a whole regarding the crystalline Form IODV succinate.

[164] Apotex disagrees. At page 8 of the 668 Patent the inventors state: "[F]orm 1 of ODV succinate has an XRPD pattern substantially identical to that shown in Figures 1 (ground Form I) and 7 (unground Form I)." At page 25 the 668 Patent states that: "[W]ithout being bound by any theory, the inventors theorize that the XRPD for the unground crystals differed from that of the ground crystals due to the preferred orientation of the unground crystals." Apotex says that Claims 8 and 9 do not cover Form I ODV-S (unground), and in large part base this on the evidence of Dr. Steed. In my view this is not the proper construction of either Claims 8 or 9. First of all, neither Claims 8 nor 9 exclude the unground Form I. Secondly, Apotex's Dr. Steed in his original affidavit did not deny the inventors' theory concerning orientation of the unground crystals: his evidence was that the skilled person would have "reservations" with it. Further, Pfizer's Dr. Atwood filed a reply affidavit that directly and very specifically addresses Dr. Steed's point and did so through the eyes of the skilled person. Dr. Atwood stated that:

> 4. Specifically, in paragraphs 158-159, Professor Steed states that the differences in the peak listings provided for the XRPD diffractograms of Figure 1 and Figure 7 exhibit differences in their 2θ values that cannot be the result of preferred orientation effects in the unground sample (Figure 7) and must mean that the materials are different. <u>However, Professor Steed relies on the lists of "characteristic" peaks the patent provides for each of these samples in Tables 1 and 6 to suggest that the peak positions are different. These lists of "characteristic" peaks do not include all of the peaks present in either diffractogram and are not intended to be</u>

> exhaustive. It is not correct to compare one against the other in order to look for differences or similarities in the peak positions. Indeed, as Professor Steed notes, preferred orientation effects can change the height (intensity) of the peaks in a XRPD diffractogram, which means that different peaks may appear to be 'characteristic' in the ground sample as compared to the unground sample.
>
> 5. A comparison of Figures 1 and 7 reveals that despite some differences in intensities that Figure 7 exhibits all of the seven characteristic peaks of Form I (peaks appear at around 10.20 2θ, 14.91 2θ, 20.56 2θ, 22.13 2θ, 23.71 2θ, 24.60 2θ and 25.79 2θ). More tellingly, it does not exhibit any additional significant peak(s) aside from those that appear in the XRPD diffractogram provided in Figure 1. In my opinion, these two XRPD diffractograms clearly represent the same form and I believe a person of ordinary skill in the art would reach the same conclusion.
>
> [Emphasis added]

[165] Dr. Steed filed a sur-reply affidavit in which he buttressed his position that the ground and unground versions of Form I are "different materials". However, I on a balance of probabilities, I accept Dr. Atwood's evidence that the "two XRPD diffractograms clearly represent the same form and I believe a person of ordinary skill in the art would reach the same conclusion."

[166] In addition, and this speaks to the construction of both Claims 8 and 9, Apotex stated in its Notice of Allegation that: "[t]he skilled person would understand that Claims 8 and 9 to relate to Form I desvenlafaxine succinate." In my view that statement reflects the intention of the inventors; in my view their intentions should be given effect through a construction that holds that the two XRPD diffractograms represent the same form, namely the crystalline Form I ODV succinate.

[167] [redacted]

[168] In the circumstances, in my view the proper construction of Claim 8 is that it covers Form I ODV (mono) succinate monohydrate (*i.e.*, the crystalline form of ODV succinate, which exhibits the characteristic XRPD peaks of Figure 1). In my view, this construction gives effect to the intention of the inventor and does so in the context of the patent as a whole.

[169] As to Claim 9, in addition to what I have stated and found regarding Claim 8, in my view this claim refers to another identifier, namely an endotherm (melting point). In my view, this claim also refers to the crystalline Form I ODV succinate. I am supported in arriving at this conclusion by Apotex's Notice of Allegation which appears to concede the point where it states, in material part, that a skilled person would "understand claims 8 and 9 to relate to Form I ODV desvenlafaxine succinate" *i.e.* the crystalline Form I ODV succinate.

[170] The parties dispute the margin of error referred to in Claim 9. Claim 9 claims "[A] compound according to claim 6 having an endotherm at about 131°C". The key word is "about". Pfizer argues that "about" means ± 2°C, therefore Claim 9 encompasses those compounds having an endotherm falling within the range of 129-133°C. Apotex says it means ± 1°C, narrowing the range to 130 to132°C.

[171] The 668 Patent defines the word "about" under the heading "Definitions" on page 4: "The term" about "generally means within 10%, preferably within 5%, and more preferably within 1% of a given value or range. Alternatively, the term" about "means within an acceptable standard error of the mean, when considered by one of ordinary skill in the art."

[172] However, I do not accept this definition applies to endotherms - if it did, then at one end of the numerical margins of error it would be ± 13, *i.e.*, a 26°C variation which is far too great a difference to have been intended by the inventors. Therefore, and in my view as a matter of construction, the definition turns on the alternate, namely "an acceptable standard error of the mean, when considered by one of ordinary skill in the art."

[173] The experts disagreed. Both Pfizer's experts, Drs. Myerson and Atwood, considered this definition and opined that the margin of error for such endotherms is up to ±2°C. Apotex's Dr. Steed while stating that the definition in the 668 Patent was ambiguous, proceeded to review the 668 Patent for claim differentiation and concluded that "about" meant ±1°C. Apotex's approach presents a serious difficulty in that the issue is not claims differentiation but the margin of error for this sort of measurement as seen by the Skilled Person. In this respect, I prefer the evidence of Drs. Myerson and Atwood which directly addressed the question as understood by the Skilled Person. Dr. Steed provided a much less satisfactory answer which in effect did not speak to the Skilled Person's appreciation of the margin of error for DSC measurements in terms of the state of the art for this sort of measurement, but very differently provided a case-specific analysis in which the answer depends how claims in this patent - or by extension, some other

patent - may be differentiated. In my view Dr. Steed did not answer the question in terms of the state of the art as well as did Drs. Myerson and Atwood. I should note that I arrived at this conclusion without regard to Pfizer's argument based on the fact that Apotex's own proposed new drug submission also speaks to a margin of error of ±2°C.

[174] I agree with Apotex that if the margin of error is ±2°C, Claim 12 also will be captured by Claim 9 and vice versa. However, in my view the inventors did not intend Claims 9 and 12 to encompass both Forms I and II. In my view, the presumption of different meanings for different claims is displaced; the intention of the inventors was to describe the same compound by reference to the different identifiers set out in both Claims 8 and 9. In my view Claims 8 and 9 should be construed to identify the same crystalline form, namely the crystalline Form I ODV succinate.

[175] Therefore I construe Claim 9 to covers Form I ODV (mono) succinate monohydrate (*i.e.,* the crystalline form of ODV succinate, which exhibits a characteristic endotherm at about 131°C (+ 2°C)).

[176] Again, this construction gives effect to the intention of the inventor and does so in the context of the patent as a whole regarding the crystalline Form I ODV succinate referred to on page 8 of the 668 Patent.

B. Construction of Claim 33

[177] Apotex says that the only debate between the parties relates to the scope of Claims 8 and 9 upon which claim 33 is dependent. Therefore I construe Claim 33 as it depends on Claims 8 or 9, use of Form I ODV succinate for the treatment of depression.

C. Construction of Claims 43 and 44

[178] Apotex says that by specifying that the use will "lower" side effects, the claim makes a comparison to a dosage form which does not limit the blood plasma level to 225 ng/ml or less; that the claim is not specific to crystal form, nor to any specific blood plasma level below 225 ng/ml; and notes with respect to the comparator, Pfizer's experts proposed an instant release formulation.

[179] To recall, this is the claim to the "sustained release oral dosage form." I agree that the claim as worded does not refer to specific crystal form, but consistent with my findings respecting the intention of the inventors and the purpose of the 668 Patent respecting claims 8 and 9, the claim should be construed with respect to the crystalline Form I ODV succinate. The other points made by Apotex should not be incorporated into the construction of this claim.

[180] In my view Claim 43 should be construed as follows: as it depends on Claims 8 or 9, use of a sustained release oral dosage form comprising Form I ODV succinate to induce an average

blood plasma level of no more than 225 ng/ml to lower the overall incidence of the specified side effects as compared to oral administration of ODV succinate not so formulated.

[181] Regarding Claim 44, Apotex says in its claims construction arguments that this claim is for an sustained release formulation containing ODV-S providing peak serum levels of up to 225 ng/ml (*i.e.*, from 0 to 225 ng/ml), and that this claim is not limited to oral formulations or to any particular form of ODV-S. I agree that this claim is not limited to oral formulations or to any particular form of ODV-S, but I see no need to add that to the claim construction as a matter of law.

[182] Therefore, Claim 44 should be construed as follows: a sustained release formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I ODV succinate) which provides average peak serum levels of up to 225 ng/ml.

3. Non-infringement

[183] I will deal with this issue claim by claim.

[184] **Claim 8**: Pfizer asserts that both of Apotex's 50 mg and 100 mg products infringe Claim 8. Apotex made no allegation of non-infringement with respect to Claim 8 except on the basis that Claim 8 is invalid and therefore cannot be infringed.

[185] Because I have found on a balance of probabilities that Apotex's allegations relating to the invalidity of Claim 8 are not justified, I find on a balance of probabilities that Apotex's allegation of non-infringement of Claim 8 is not justified.

[186] **Claim 9**: Pfizer asserts that both of Apotex's 50 and 100 mg products infringe Claim 9. Apotex defends on the bases that (1) Apotex's products irrespective of dosage do not fall within the scope of this claim and (2) that Claim 9 is invalid and cannot be infringed.

[187] Apotex's allegation of non-infringement relating to Claim 9, other than that depending on a finding that Claim 9 is invalid, is based on the meaning of "about" which I have just discussed under "Claims Construction", above. Apotex says that if the Court accepts Apotex's construction of "about 131°C" (namely, 130°C to 132°C) , Apotex's proposed product as set out in its new drug submission, which has a melting point below 130°C, does not infringe Claim 9 and therefore Apotex's allegation would be justified in this respect. The converse is also true, namely that if the Court accepts Pfizer's construction of "about 131°C", Apotex's proposed product will infringe.

[188] I have found that the proper construction of Claim 9 entails a margin of error is ±2°C, producing a range of endotherms between 129°C and 133°C.

[189] According to Apotex's Dr. Steed, the endotherms of the API in Apotex's proposed new drug "exhibited endotherms at 129.33°C, 129.18°C, 129.34°C, and 128.96°C".

[190] Therefore I find on a balance of probabilities that Apotex's products irrespective of dosage fall within the scope of Claim 9. I have also found on a balance of probabilities that Apotex's allegations relating to the invalidity of Claim 8 are not justified. I find on a balance of probabilities that Apotex's allegation of non-infringement of Claim 9 is not justified.

[191] **Claim 33**: Pfizer asserts that both of Apotex's 50 mg and 100 mg products infringe Claim 33. Apotex made no allegation of infringement with respect to Claim 33 except on the basis that Claim 33 is invalid and therefore cannot be infringed.

[192] Because I have found on a balance of probabilities that Apotex's allegations relating to the invalidity of Claim 33 are not justified, I find on a balance of probabilities that Apotex's allegation of non-infringement of Claim 33 is not justified

[193] **Claims 43 and 44**: Pfizer only asserts that Apotex's 50 mg product would infringe Claims 43 and 44. Pfizer does not dispute that Apotex's proposed 100 mg product will not infringe Claims 43 and 44. Apotex defends on the basis that Claims 43and 44 are invalid and thus cannot be infringed by its 50 mg product.

[194] Because I have found on a balance of probabilities that Apotex's allegations relating to the invalidity of Claims 43 and 44 are not justified, I find on a balance of probabilities that Apotex's allegation of non-infringement by its 50 mg product of Claim 43 and 44 is not justified.

[195] I find on a balance of probabilities that Apotex's allegation of non-infringement by its 100 mg product of Claims 43 and 44 is justified.

[196] A patentee will prevail even if only one claim of a patent is found to have been infringed: *Hughes & Woodey on Patents,* LexisNexis, loose leaf 2017, vol. 1, para 38 citing to *Arctic Cat Inc v Bombardier Recreational Products Inc,* 2016 FC 1047 at para 211. In this case I have found that Apotex's proposed product will infringe several of the claims in the 668 Patent.

[197] Therefore I conclude on a balance of probabilities that Pfizer has established that Apotex's allegation of non-infringement is not justified.

4. Obviousness

A. Introductory comments and summary

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

Invention must not be obvious	**Objet non evident**
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	**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) information disclosed more	a) qui a été faite, plus d'un an

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	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) 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.]	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.]

[199] One of the central issues in this case is obviousness, and its ancillary doctrine, obvious to try. 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 668 Patent. I have concluded that viewed through the eyes of the Skilled Person, the invention claimed in the 668 Patent, and in particular the inventive concepts of Claims 8, 9, 33, 43 and 44 were not obvious and were not obvious to try.

[200] 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.

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

B. Legal principles in the obviousness inquiry and the *Sanofi* decision

[202] 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*].

[203] That said, after the hearing of this case, the Supreme Court gave judgment in *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36 [*AstraZeneca*], dealing with the Promise Doctrine. In post-hearing filings on the impact of *AstraZeneca* (which I will discuss in detail under the heading of inutility), Apotex argued that the law of obviousness was changed by *AstraZeneca*. I am not persuaded; had the Supreme Court intended to restate the law of obviousness in *AstraZeneca* it could have done so and said do but it did not. It does not appear to me that the Supreme Court intended to opine on obviousness when dealing with the utility arguments it addressed in *AstraZeneca*. While the obviousness inquiry starts with the claims, it is trite law that claims are to be read with a view to the patent as a whole. That the Court must "identify the inventive concept of the claim" in question or if that cannot readily be done, construe it, is demanded at the second step of the Sanofi inquiry, as I will address shortly. Nothing in *AstraZeneca* says that different claims may not have different inventive concepts, and indeed the Supreme Court of Canada said that it is possible for each claim in a patent to disclose a separate invention: *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60 at para 64. Claims construction allows the Court to read the claim in the context of the patent as a whole, including

the description and other claims, and the disclosure may be considered to assist in understanding the claims or to dispel ambiguity.

[204] Therefore, as indicated, I prefer to rely on *Sanofi* for the law of obviousness.

[205] For convenience of reference and because of its centrality on this issue, I will set out in its entirety the relevant part of the *Sanofi* decision 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.]

[206] 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.

[207] 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.

[208] According to *Sanofi's* 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."

[209] 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."

[210] It recapped these parameters in para 66 stating: "[F]or 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 including *Atazanavir* and *Beloit*

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

[212] 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.]

[213] 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.

[Emphasis added.]

[214] In *Eli Lilly v Mylan*, 2015 FCA 286, per Dawson J.A., the Federal Court of Appeal at para. 4, declined to agree that the obvious to try test should be "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 at para. 4 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."

[215] Shortly before the hearing in the case at bar, the Federal Court of Appeal released *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76 [*Atazanavir*]. The parties included references to *Atazanavir* in their submissions.

[216] 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].

[217] 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."

[218] 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 F.C.R. 459 at para. 105.

[219] In this connection the Federal Court of Appeal in *Atanazavir* also referred to the test for obviousness prior to *Plavix* which test had been set out by the Federal Court of Appeal in *Beloit Canada Ltd v Valmet OY* (1986), 64 N.R. 287, 8 C.P.R. (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.

[220] 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.

[221] 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.]

[222] In *Atanazavi*, 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

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

1. (a) Identify the notional "person skilled in the art"

[224] A patent is addressed to the "Person of Ordinary Skill in the Art" [Skilled Person], who I previously defined in the following terms:

> [38] A patent is addressed to this notional Skilled Person, who is "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. The "unimaginative and uninventive" language is found in *Beloit Canada Ltd v Valmet OY* (1986), 8 C.P.R. (3d) 289 (F.C.A.) [*Beloit*], where the Federal Court of Appeal refers to the "unimaginative skilled technician", and *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at para 81, where the Supreme Court refers to inventiveness as foreign to the Skilled Person in the obviousness analysis. In my view, the Federal Court retained these concepts in its interpretation of the skilled technician in patent law: *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 (Dawson, J.A.).
>
> *Gilead Sciences, Inc v Canada (Health)*, 2016 FC 856.

[225] In this case, the parties take the following positions on the qualities of the Skilled Person, which would in this case be a person or team of people:

> Pfizer's position: The 668 patent is directed to those skilled in the arts of solid state chemistry, pharmaceutical formulation and development, pharmacology and pharmacokinetics.
>
> Apotex's position: The 668 patent addresses solid state chemistry, pharmaceutical formulation and development, pharmacology, pharmacokinetics, and the treatment of disease and conditions. By definition the skilled addressee would have skills in these areas.

[226] I take it as a given that a Skilled Person has skills in their respective areas. Therefore, the parties disagree only on whether the Skilled Person would have skills in the treatment of disease and conditions, which is what Apotex says; Pfizer disagrees. However, Apotex's Dr. Parr agreed that "the 668 Patent is not necessarily directed to a medical doctor", and added that pharmaceutical scientists understand that their purpose is to formulate an active ingredient in a way that allows it to be both therapeutically effectively and safe when used in a clinical setting. In cross-examination Dr. Parr stated that a Skilled Person team without an MD was an option. In fact, the only expert with a medical degree (Pfizer's Dr. Blier) deposed that medical expertise is

not required of the Skilled Person. Dr. Blier added that "in general, medical doctors are concerned with the treatment of patients in a clinical setting and not with the formulation of drugs -- that is the work of a person of skill in pharmaceutics." I agree.

1. (b) Identify the relevant common general knowledge of the Skilled Person

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

[228] In my view, as of February 2001, general methods and techniques to make salts and crystals and prepare sustained release dosage forms were known and published. The skilled person would also know that ODV had been disclosed to be an active metabolite of venlafaxine and a member of a class of compounds in several patents including the US 186, WO 551 and CA 540. And they would know that ODV was useful to treat depression. The prior art disclosed ODV both as a free base and a fumarate salt, and the Skilled Person would know that other pharmaceutically acceptable salts (including succinate, among at least eleven (11) others as set out in US 186 at column 2, ll. 35 and following; 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.

[229] However, Pfizer is correct in stating that while the prior art explicitly disclosed ODV as a free base and a fumarate salt, and ODV succinate as a potential salt, no crystal form of that salt let alone the crystalline Form I ODV succinate had ever been expressly disclosed, made or

characterized. Also, none of the prior art teaches the successful preparation of a succinate salt of ODV nor does it teach, more importantly for this case, the successful preparation of Form I ODV succinate, and nothing in the prior art discloses any of the properties or either ODV succinate or Form I ODV succinate.

[230] In my view, the number of experiments required to move from the acceptable pharmaceutical salts to the Form I ODV succinate was extremely large as deposed by Dr. Myerson at para 102 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 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 not 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."

[231] 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 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.

[232] The Skilled Person would know generally of the existence of crystalline and polymorph screening, and as Apotex's expert put it, that crystal and polymorph screening was "specialized" work that had to be done. As Dr. Park deposed, polymorph screening was not rote work, was difficult and in her experience 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 had 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.

[233] 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, as set out in para 126 and following of these Reasons. I appreciate that Dr. Park is a named inventor in the 668 Patent, but this did not detract from her evidence.

[234] Dr. Myerson deposed:

> **Choosing an Appropriate Salt**
>
> 72. 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.
>
> 73. 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).
>
> 74. 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.
>
> 75. <u>The salt selection and formation process is highly unpredictable. Indeed, one cannot predict prior to actually</u>

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.

76. 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.

77. 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

78. 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.

79. 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.

80. 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.

81. 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.

82. 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.

83. 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).

84. 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

85. 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).

86. 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.

87. 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

89. 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.

90. 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.

91. 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.

92. 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.

93. 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.

94. 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

98. 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.

99. 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.

100. 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.

101. 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.

102. 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.

103. 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.
>
> 104. 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.
>
> 105. 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.]

[235] 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.

[236] This was not only the evidence of Pfizer, but of Apotex as well.

[237] Evidence offered by Apotex's Dr. Bastin confirmed that looking at the 186 Patent and Can 540 Patent, even if the Skilled Person performed a salt screen he or she would not know in advance which salts would be formed from the screen. Further, neither Patent gave the skilled person any more information about which salts of ODV could be made than the other prior art. Dr. Bastin likewise agreed that the 851 Patent does not identify which salts are necessarily referred to.

[238] The evidence further confirmed that choosing the appropriate salt can be a very difficult task, which in my respectful view required judgment. Dr. Steed was referred to an article which stated: "[C]hoosing the appropriate salt, however, can be a very difficult task, since each salt imparts unique properties to the parent compound." Dr. Steed was asked if that was "something that the skilled reader would observe as being part of the art in 2001. Correct? A. Yes and the keyword here is "choosing", that making a choice can be a difficult task because very often different commercial drivers, depending upon a particular way in which a medicine is to be sold."

[239] To the same effect was another article (Bighley) put to Dr. Steed, which said: "[A]lthough attempts have been made to apply 'decision analysis' and 'potential problem analysis' to select salts and help predict salt performance [1], the choice of which salt to use remains a difficult decision." Dr. Steed testified:

> Q. That is certainly something that the skilled reader reading this document in 2001 would observe and make a note of. Correct?

> A. Once again, you are referring to the choice being the difficulty here and in fact what this article is doing is providing, as he says, a decision tree to help with that choice.

[240] It seems to me that Pfizer is correct in stating that there was no generally accepted procedure of selecting a salt form because each procedure is based upon the structure of each particular drug form.

[241] This was confirmed by Apotex's Dr. Steed who agreed that teachings in a 1994 textbook was part of the prior art in 2001. The textbook stated: "[Al]though the importance of using the optimal salt form of a compound in dosage form design is well-recognised there is no generally accepted procedure of selecting such a form during the drug development." Dr. Steed explained the meaning of this passage:

> Q. Have I read that correctly?
>
> A. You have, that is because each procedure is based upon the particular drug substance in question.
>
> Q. I was just asking whether or not I had read it correctly?
>
> A. Your reading was accurate.
>
> Q. Thank you. And this was something that a skilled person would have read and observed in 2001. Correct?
>
> A. Yes, this is part of the state of the art in 2001.

[242] The following passage from a textbook relied upon by Dr. Steed stated: "[T]his review is intended to provide a strategic approach to remove much of this uncertainty by presenting concepts and ideas in the form of flow charts rather than a set of guidelines or regulations. This

is especially important because each individual compound has its own peculiarities which require flexibility approach." Dr. Steed gave the following answers regarding this passage:

> Q. Stopping there, and a skilled reader would make note of that observation and statement on 2001. Correct?
>
> A. Yes, this is a 1995 article, part of the state of the art, in which Byrn is providing a systemic approach to addressing regulatory concerns over solid form.
>
> Q. Right, and he is saying that because each compound has its own peculiarities an investigator must use some flexibility in the approach. Correct?
>
> A. That is what he says, yes, and what he means by that is that you need to consider the actual structure of the drug substance itself in designing the screening.

[243] The foregoing deals with the salts. The situation regarding crystals is, if anything more complex, and further from the capabilities of the unimaginative uninventive Skilled Person in my respectful view, based on the experience of Dr. Park which I have accepted and that of Dr. Myerson referred to at para 234 above. Apotex's witnesses confirm a number of points, a central one being the fact that identification of crystals was not predictable. Dr. Steed agreed that the Skilled Person in 2001 "cannot predict in advance how many crystal structures of a compound might be stable under a given set of conditions." While he then testified that "is possible to make predictions about how many crystal forms there might be computationally", he did not share any such computations in his affidavit, and later agreed that crystal structures were in fact not predictable. In 2009 he authored a book in which he stated that in general crystal structures are not predictable: "[D]espite the fact that, in general, crystal structures are not predictable, a number of attempts, some of them increasingly successful, have been made to

address the problem from a computational standpoint." Apotex's Dr. Steed testified that: "[T]he trick is knowing which ones of those will actually form in practice. In other words, finding the conditions to produce them." He confirmed that if crystal structures were generally unpredictable of 2009, they were also generally unpredictable to the Skilled Person as of 2001. He later confirmed that in 2001 the computational approach did not work in 2001, "… the field in 2001 did not really progress by calculating a crystal structure in advance, it is much more simple to simply crystallise the compound and analyse its structure experimentally."

[244] Moreover, polymorph screening was not only difficult, but seen as time-consuming and expensive according to Dr. Steed who wrote in 2012 concerning crystal forms of theophylline, polymorphs and hydrate: "[D]iscovery of the full range of crystal forms of any given compound is usually time-consuming and expensive, and even after extensive screening it is difficult to be certain that the process is complete and every possible form has been identified." Dr. Steed also wrote: "[I]t is increasingly apparent that many compounds can exist in more than one crystal form, and identification and analysis of every form (particularly the thermodynamically stable form under a given set of conditions) is essential for manufacturing, storage, and intellectual property considerations."

[245] Apotex makes a great number of other assertions concerning what a Skilled Person would know of the common general knowledge. To save repetition I will deal with these under Question 1 of *Sanofi*'s obvious to try analysis later in these Reasons at para 300.

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

[246] Identifying the inventive concept is the next step in the obviousness analysis outlined 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*, "what is claimed in the patent" and "the invention" are synonymous with "inventive step" and "the solution taught by the patent". The solution taught by the patent, also known as the inventive concept is to be assessed in respect of each claim at issue (claim by claim), which emphasizes that different claims may have different inventive concepts.

[247] This second point, the solution taught by the patent, also known as the inventive concept is to be assessed in respect of each claim (claim by claim) at issue: *Sanofi* at para 67. I accept that different claims may have different inventive concepts: *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."

Apotex's Dr. Steed was instructed to the same effect; he said in cross-examination: "[I] was told the inventive concept is to be discerned from the language of the claims with the understanding that the individual claims may have different inventive concepts to them, so yes, it is a claim-by-claim basis." Apotex's Dr. Bastin testified that "novel crystalline forms are inventions above and beyond the identification of a salt."

[248] **Claims 8 and 9**. Both Claims 8 and 9 cover Form I ODV (mono) succinate monohydrate, that is, the crystalline Form I 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 identifying properties are not the inventive concept, nor are they the solution taught by the 688 Patent.

[249] In my respectful view, the solution taught by these two claims, heir 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 these two claims in the 668 Patent is the novel crystal Form I ODV succinate.

[250] Apotex disagrees and says the 668 Patent teaches that the solution to this problem is ODV succinate in any form, and further that ODV succinate is the single inventive concept of

the claims. With respect, I am unable to agree. It is well established that in construing the claims one must read the patent as a whole, a point Apotex's Dr. Steed conceded. However, Dr. Steed, who advanced the single inventive concept in connection with all asserted claims, did not discuss the following statement in the 668 Patent itself, which says at page 5, that "[E]ach polymorph forms another aspect of the invention." Dr. Steed agreed, however, that by this statement in the 668 Patent, the "inventors are clearly telling the reader that polymorphic forms would be different aspects of the invention." Apotex's Dr. Parr in cross-examination on the same statement in the 668 Patent, agreed with the proposition that:

> Q. [B]y 'another,' when it says, 'another aspect of the invention,' it means an aspect of the invention in addition to the invention of the novel salt?
>
> A. Yes, ma'am.

[251] Based on this evidence and the clear language of the statement in the 668 Patent that "[E]ach polymorph forms another aspect of the invention", I am confirmed in my view that the inventive concept or the solution taught by these two claims in the 668 Patent is the novel crystal Form I ODV succinate. I also reject Apotex's single inventive concept argument.

[252] **Claim 33**. 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 I ODV succinate for the treatment of depression.

[253] 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.

[254] I have rejected the single inventive concept argument.

[255] **Claim 43**. 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." Properly construed, this claim means: as it depends on claims 8 or 9, use of a sustained release oral dosage form comprising Form I ODV succinate to induce an average blood plasma level of no more than 225 ng/ml to lower the overall incidence of the specified side effects as compared to oral administration of ODV succinate not so formulated.

[256] The inventive concept of claims 43 and 44 is a sustained release dosage form comprising the new crystalline Form I ODV succinate that has specific pharmacokinetic characteristics namely 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.

[257] I have rejected the single inventive concept argument.

[258] **Claim 44**. 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." I have construed it as a sustained release formulation comprising O-desmethyl-venlafaxine succinate (in any form, including Form I ODV succinate) which provides average peak serum levels of up to 225 ng/ml.

[259] 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.

[260] Taken together, 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 refers to lowering the incidence of adverse side effects while Claim 44 does not; both reference a peak blood plasma level of less than 225 ng/ml.

[261] I have already rejected the single inventive concept argument.

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.

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

i. Claims 8 and 9

[263] In my respectful view, the Skilled Person would not know nor could he or she predict that ODV succinate salt would form as a solid, whether that solid would form as a crystal, or what the properties of a 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 prior art.

[264] 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.

[265] In my view therefore 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

[266] 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.

[267] 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.

[268] For the same reasons that Form I ODV succinate was not more or less self-evident, in my view, neither was its use to treat depression.

[269] 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

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

[271] 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. Claim 44 does not refer to side effects.

[272] 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 non-sustained release administration. With respect, I agree.

[273] I have found that neither ODV succinate nor any of its forms or properties were known, predicted or predictable. 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 with Claim 33, the prior art also taught and the Skilled Person knew that every new solid form had its own set of unknown, unpredicted and unpredictable properties.

[274] 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.

[275] While 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 release administration, 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 sustained release formulation. Nor was it obvious or predicted or predictable that Form IODV succinate would have the appropriate stability, 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 sustained release formulation of ODV succinate would result in blood plasma levels below 225 ng/ml while maintaining therapeutic concentrations as per both Claims 43 and 44.

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?

5. Apply the definition of obvious before *Sanofi*

[276] 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*.

[277] 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.

[278] I appreciate Apotex'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. I have already accepted and prefer the evidence of Dr. Myerson on the common general knowledge regarding the matters of salt screens and crystalline and polymorph screening as set out above at paras 234 and 278 of these reasons. I have also accepted the experience-based evidence of Dr. Park in this connection, see para 124 and following, which corroborates that of Dr. Myerson. Dr. Myerson concluded:

> 102. 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.

103. 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.

104. 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.

105. 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.]

[279] In these circumstances, and 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, would not have come directly and without difficulty to the solution taught by the 668 Patent, namely the novel crystalline form of ODV succinate referred to as Form I.

[280] 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. Further, 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 predictable result.

[281] 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, this finding applies also to Claims 33, 43 and 44.

[282] The obviousness inquiry does not end here. At this point, having looked at obviousness using the *Beloit* test, the Court must follow the balance of the steps suggested by *Sanofi*. The

Court must now consider the applicability of, and if appropriate, review the matter against the 'obvious to try' test.

6. Consider the doctrine of obvious to try

[283] 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 at para 68: "When Is the 'Obvious to Try' Test Appropriate?" In answer it said at para 68: "[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."

[284] This case is one in 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.

[285] In doing so, I note the introductory guidance set out in *Sanofi* at para 64: "[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 described as "useful guidance" by the Federal Court of Appeal in *Apotex Inc v Pfizer Canada Inc*, 2009 FCA 8 at para 26.

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

[287] 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.

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

7. 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?

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

[290] 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.

[291] I agree with that summary because it is borne out in the extract from the affidavit of Dr. Myerson set out at paras 234 and 278 of these Reasons, whose evidence was corroborated by the experience of Dr. Park as set out at para 124 and following of these Reasons. Dr. Myerson concluded with respect to the crystallization and polymorph screening, with apologies for repetition:

> 103. 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
>
> 104. 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.

> 105. 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.

[292] 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 there were not because the number of potential experiments was in fact extreme 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.]

[293] This fact was confirmed by Dr. Park's experience who deposed at para 34 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."

[294] 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 engaging in a research program, on the facts of this case, there were no identified predictable solutions.

[295] Apotex argues that salt screens and crystallization and polymorph screening constituted routine experimentation known to the Skilled Person, and that knowledge together with a large number of other factors alleged to be known to the Skilled Person made it more or less self-evident that Form I ODV succinate, *i.e.*, what was being tried, ought to work.

[296] 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. I disagree with the position advanced by Apotex because 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*.

[297] 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 those arguments, said:

> [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.
>
> [Emphasis added.]

[298] 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 salt screens and crystallization and polymorph screening research programs it might be possible to identify crystals and polymorphs. 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 place, 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. But mere possibilities are not sufficient.

[299] 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." [para 85] 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 facts of this case.

[300] Apotex argued that the Skilled Person would have knowledge of numerous other matters, which taken together would have led him or her to the solution taught by the 668 Patent, *i.e.*, Form I ODV succinate. I will attempt to list them, followed by my observations:

A. The skilled person knew that the properties of medicinal compounds were typically improved by forming salts. Court comment: it was known that some compounds might form salts while others might not and that if salts formed they might entail improved properties. That was a hoped for result.

B. Further, ODV had been the subject of previous patents, which patents taught and claimed salts (and solvates) of ODV generally. Court comment: I agree.

C. It was known that such salts typically crystallize into one or more different solid forms, each one having somewhat different pharmaceutical properties. Court comment: I disagree: crystallization was not a certainty, some might crystalize, some might form into amorphous forms, and some may do neither. [redacted]

D. For example, ODV-S, as a salt, would be expected to be more soluble than ODV free base, and generally speaking, increased solubility was correlated with increased oral bioavailability. Court comment: I disagree because this result was not known or predicted and required testing and experimentation.

E. The skilled person knew that changing the form (i. e. salt/polymorph) was a way to change the properties of a drug relevant to its formulation and use. Court comment: this is correct only so far as it goes because it was equally known that no crystal might form, and in any event no one knew or could predict any resulting properties.

F. Skilled persons would, as a matter of routine, prepare a number of different salts under various conditions and verify the properties of these salts in parallel, that is, conduct a "screen". This is among the most routine tasks for those in the industry. There is always an expectation that salt selection will lead to crystalline forms. Court comment: I disagree: I decline to find salt screens among "the most routine tasks".

Moreover the test of "fair expectation of success" was not approved in *Eli Lilly v Mylan*, 2015 FCA 286 at para 4.

G. Experts from both parties agreed that virtually all salts will be isolatable as crystals. Solubility, permeability, bioavailability, crystallinity and hygroscopicity were properties that would have been evaluated as part of the screen. The skilled person would expect that one or more salt forms having suitable properties for development would be identified. Court comment: I disagree. The Skilled Person would know that some salts would not crystallize; [redacted] What the Skilled Person would see was a course of experimentation in the nature of a research program.

H. The skilled person would characterize the solid state form by XRPD and DSC as an ordinary part of pharmaceutical development. Court comment: I agree. I would note that identifying the XRPD is simply one method of characterizing a substance.

I. The skilled person would always expect that ODV would be useful in the treatment of depression irrespective of its salt or polymorphic form. Court comment: I disagree; one may say that ODV was known to be useful in the treatment of depression; for use in treatment as drug that did not require metabolization in the body, ODV would have to be formulated into a drug with solid state stability, and a drug was soluble, permeable and bioavailable; no Skilled Person could identify which if any salt would qualify let alone which if any crystal would have the

appropriate mix of properties for development as a drug, let alone its effective therapeutic dosage(s).

J. ODV was understood to be a basic compound. As such, it was known that ODV would be made into a salt by reacting it with an acid. The skilled person would screen a group of acids known for their use in creating pharmaceutically-acceptable salts. Court comment: I agree, although nothing in the prior art pointed specifically to ODV as opposed to other acceptable salts.

K. The skilled person would know that acids having a pKa of 2-3 units lower than that of ODV would form a salt. The skilled person would include succinic acid in his or her screen. Court comment: I agree.

L. Succinic acid was a common acid used to form salts of pharmaceuticals, has a pKa within 2-3 units of ODV's, and repeatedly appeared in the lists of possible salts for ODV in the prior art. In addition, it was known that the fumarate salt of ODV had been prepared and was crystalline. Succinic acid is similar in structure to fumaric acid. Court comment: I agree.

M. Given the similarity in structure, it was expected that succinic acid would also form as a crystalline solid. Additionally, succinic acid is more soluble than fumaric acid, and it was thus expected that ODV-S would be more soluble than ODV fumarate. Court comment: I disagree; these are matters that the Skilled Person knew would entail detailed and specific experimentation as part of a research program.

N. The solvents and conditions that would yield the succinate salt of ODV, including Form I, would be those used routinely. Court comment: the Skilled Person could neither identify nor predict Form I ODV succinate.

O. Typically, the most stable form of crystal would be the one most likely to form in the screen, and would be the least likely to undergo a crystal form change in the formulation process. Court comment: by definition the most stable form of crystal would be the least likely to undergo a change.

P. The generally accepted practice was to prepare and use "the most stable" crystal form (polymorph) of a crystalline salt. [redacted]

Q. No special steps were needed to arrive at Form I. Court comment: I disagree; while what became known as Form I ODV succinate was developed by Wyeth using its domestic and international facilities, that was preceded by pro-drug experiments and work on other salts including the fumarate salt. The fact remains that the salt screen work did not have an identified and predictable outcome; ODV succinate the salt had never been made before. I do not consider SSCI's specialized polymorph screening to be routine work, nor was the overall drug development program including work on a prodrug and other unsuccessful salts routine experimentation of the type performable by the unimaginative uninventive Skilled Person. Work in this regard

was in the nature of a research program especially when the *in vitro, in vivo* and human tests and experimentation are considered as they must be.

R. Once a useful salt was identified, the skilled person would choose a formulation to deliver the medicine in the manner appropriate for treatment. If an instant release of the drug was needed, immediate release compositions would be prepared. If a lower but sustained release was desired, a sustained release composition would follow. This was all routine work in the development of a new drug. ODV salts were identified as being particularly suited for inclusion in a sustained release formulation due to ODV's relatively long half-life. Prior art (e.g., WO 955, WO 851, EP 374 and US 186) disclosed the preparation and use of oral dosage forms containing ODV and its salts (including ODV-S) for use in the treatment of CNS disorders. Sustained release oral dosage forms, including those previously described for use with venlafaxine or as conventional sustained release oral formulations were said to be advantageous formulations because they would control the blood levels of the drug and therefore reduce the occurrence of side effects associated with use of venlafaxine, including in particular nausea and headache. Preparing and modifying these formulations to vary the drug's pharmacokinetic parameters was routine work for a formulator. Court comment: I disagree: the prior art did not disclose either the ODV succinate or Form I ODV succinate let alone the sustained release version with the pharmacokinetic properties claimed in Claims 43 and 44. Much of this assertion is argumentative and contrary to the evidence I have accepted of Dr. Myerson and others and the experience of Dr. Park.

S. The skilled person would be motivated to prepare ODV-S with the expectation that it would form a crystalline salt that would be useful as a medicine. Court comment: I disagree; there was no motivation in the prior art to prepare either the succinate salt let alone crystalline Form I ODV succinate.

T. Once formed, the skilled person would determine its solubility, permeability, bioavailability, crystallinity, hygroscopicity and stability and would characterize its solid state forms by DSC and XRPD. Court comment: I agree; the key is "once formed" which was neither predicted nor predictable and in respect of which the Skilled Person foresaw a research program.

U. In so doing, he or she would obtain ODV-S, including Form I ODV-S, would measure its XRPD and its endotherm, all without inventive effort. Court comment: I disagree because this is the product of several previously rejected premises.

V. Claims 33 is also obvious. In addition to the above, the Skilled Person knew that ODV-S would be useful for the treatment of depression. Neither the salt nor the polymorphic form imparts the therapeutic properties of ODV. The Skilled Person would know that, when administered, the salt would dissolve and dissociate from the ODV, lose its solid form, and be available in the body to treat depression. Court comment: I disagree; Claim 33 depends on Claims 8 and 9 and to the extent they are not obvious, Claim 33 is not obvious. Claims 8 and 9 were not obvious nor obvious to try therefore neither was Claim 33.

W. Claims 43 and 44 are also obvious for the same reasons. The Skilled Person also knew that the higher the Cmax, the greater the incidence of side effects. It was self-evident that a formulation that induces a Cmax of less than 225 ng/ml (e.g., 50 ng/ml) would have lower side effects than formulations which did not. The Skilled Person also knew that the Cmax could be decreased by administering ODV-S in a sustained release oral dosage form as discussed above. While the prior art did not disclose that an ODV dosage form Cmax ought to be less than 225 ng/ml, this information was easily ascertained through the use of commercial software and available pharmacokinetic data derived from Effexor XR or pharmacokinetic modeling techniques. Court comment: I disagree with this line of argument because Claims 43 and 44 depend on Claims 8 and 9; to the extent Claims 8 and 9 were not identified or predicted in the prior art and could not be known to the Skilled Person, the same must be said of Claims 43 and 44.

X. In any event, the 225 ng/ml C. value is of no practical significance to the working of the claim 43 and 44 formulations because this value was arrived at arbitrarily and in an unexplainable manner. Court comment: this submission has no merit as discussed at para 110.

[301] While I have dealt in summary fashion with each of the Apotex's prior art arguments, the more fundamental problem with these arguments is that they are contrary to the expert evidence I have accepted. That aside, even if all of these arguments are accepted as being in the prior art,

contrary to my finding, in my view they set up the much the same situation as was 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.

[302] 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." [para 85] As I understand it, knowing a host or multiplicity of different facts and procedures does not necessarily lead to the conclusion that it was obvious to try to find everything that could be made based on those facts and procedures. This is because, as *Sanofi* confirms at para 65: "[I]f 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."

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

discovery of Form I ODV succinate was self-evident from the prior art and the common general knowledge.

[304] In my view, these considerations under this heading point against a finding of obvious to try in this case.

8. 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?

[305] 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 234 and 278. I also have accepted Dr. Park's experience-based evidence on crystallization and polymorph screening - para 124 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.

[306] Again by analogy 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 appears stronger than that in *Sanofi* against obviousness to try, because here there is evidence which I accept on a balance of probabilities that the salt ODV succinate in fact would *not* work. This evidence was based on the fact that ODV fumarate, another salt of ODV, had not worked. Because ODV in its dissociated state, *i.e.*, separated from the ODV fumarate salt once dissolved,

did not work when introduced into the body, it was logical to expect that a different salt, namely ODV succinate, also would not work, because the ODV dissociated from the succinate salt would be the same as the ODV dissociated from the fumarate salt. If one did not work it was logical the other would now work. I also accept Dr. Shah's evidence of [redacted] The nature of the work seen in this context was uphill.

[307] 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.

[308] 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 in [redacted], rats, dogs and humans.

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

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

[310] 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.

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

[312] Pfizer's position is that beyond a general statement about the possibilities 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 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.

[313] 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. That is the same situation 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.

[314] I note also that *Sanofi* dealt with a genus patent, where, as the Supreme Court stated at para 90, “selection might be expected”, but nonetheless Sanofi found no motivation in the prior art: neither do I. Apotex accepts this is not a selection patent.

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

10. What is the course of conduct which was followed which culminated in the making of the invention?

[316] 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.

[317] I agree with Apotex that the salt form ODV succinate was made as a new composition of matter [redacted] However, and without doubting its relevance, the time taken to make a new invention is only one factor. This is particularly the case given the evidence that this particular salt and crystalline form was not 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.

[318] [redacted]

[319] Moreover, the invention story 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 experimentation began, including work on other salts including the fumarate salt, and the work directed towards developing a pro-drug - which pro-drug work the parties agree took place. It is also to 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. 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.

[320] [redacted]

[redacted] But that was neither predictable nor predicted. Again, it is but one factor. More importantly, the major purpose of SSCI's involvement was that extensive additional testing was necessary to determine whether there were other forms of ODV succinate, and if so which form of ODV succinate was the most stable, *i.e.*, the best candidate for further drug development. The fact that the new crystalline composition of matter was made before Wyeth engaged SSCI does not detract from the facts that a) the experimentation required to get to that point was more than routine in this case and b) that further experimentation was required from the specialists at SSCI.

[321] On balance, and in my respectful view, the actual course of conduct in this case entailed more than routine experimentation; in my view it was a research program. 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.

[322] 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 appropriate:

> 137 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 para 89).

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

11. Conclusion on obvious to try regarding Claims 8 and 9

[324] 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.

12. Conclusion on obvious to try regarding Claims 33, 43 and 44

[325] 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.

13. Consideration of the guidance for obvious to try analysis set out in *Sanofi*

[326] I have made these findings without specific reference to the guidance set out at the start of the obvious to try outline in *Plavix 1*. There, the Court stated that the obvious to try doctrine must be “approached cautiously” and is “only one factor to assist in the obviousness inquiry”, “not a panacea” at para 64.

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

[328] I turn to the Supreme Court's considerations in *Sanofi* 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] This guidance confirms my finding on a balance of probabilities that Apotex's allegation of obvious to try is not established.

[329] In summary, the guidance provided by the Supreme Court with respect to obvious to try supports the conclusions that Form I ODV succinate was not obvious to try.

14. Conclusion on obviousness

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

5. Inutility

[331] The statutory basis for the proposition that a patent is invalid for inutility, or put another way, that it lacks utility, is set out in the *Patent Act* at s 2 where it is enacted that an invention must be "useful":

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)*	***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)*

[Emphasis added.] [Soulignement ajouté.]

[332] Previously, the discussion of utility would have started out by 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* originally requesting revised submissions on utility. Apotex asked that it be allowed to file submissions on anticipation and obviousness in addition to utility, and as a consequence I asked the parties to file submissions "concerning" the *AstraZeneca* decision and the case at bar. Both parties filed main and responding submissions.

[333] Pfizer summarized its arguments on utility this way:

> 1. In *AstraZeneca Canada Inc. v. Apotex Inc.* ("*AstraZeneca*"), the Supreme Court significantly modified the law of utility by expressly overturning the "Promise Doctrine," which it found to be "unsound," "excessively onerous," and "counter to the scheme of the [Patent Act]." Instead, the 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* (the "Act"), even if multiple uses are disclosed or described.
>
> 2. Even under the now-rejected "promise" approach, the Asserted Claims of the 668 Patent had sufficient utility. Therefore, under the new framework, with its substantially lower threshold, Apotex's allegations of inutility cannot be justified. While the 668 Patent may disclose multiple uses relating to 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, which the inventors demonstrated prior to the relevant date. This is a complete answer to Apotex's allegation that the subject matter of claims 8 and 9 lack utility under section 2 of the Act.
>
> 3. Apotex 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, Apotex's argument that claims 8 and 9 lack utility was based on its allegation that these claims were associated with a number of promises, including promises relating to comparative properties of the salt, and the reduction of side-effects. Now that it is clear that any utility is sufficient to support a claim, Apotex's allegation cannot succeed.
>
> 4. In *AstraZeneca*, the Court reminded parties that patents are designed to provide inventive solutions to practical problems. That is precisely what the 668 Patent does. The inventors had a problem: prior forms of ODV exhibited unfavourable properties for drug development. They conducted experiments to try to solve, and ultimately succeeded in solving, that problem. Through those experiments, they discovered a new salt (ODV succinate) with improved properties and a novel crystal form (Form I ODV succinate) that was sufficiently stable for development. Based on *AstraZeneca*, the stability of Form I, and therefore its suitability for pharmaceutical development, is sufficient utility to support claims 8 and 9, regardless of what other uses the patent specification may disclose.
>
> 5. Finally, the only issue before the Supreme Court in *AstraZeneca* was the utility required under section 2 of the Act. The Court did not address the law of either obviousness or anticipation and nothing in the *AstraZeneca* decision alters the tests for obviousness or anticipation it previously set out in *Sanofi-Synthelabo*.

[334] Apotex summarized its utility arguments (it also raised obviousness and overpromising but did not revisit anticipation) as follows:

> 15. In *AstraZeneca*, the Supreme Court held that the "promise of the patent" doctrine as described by the Court is not the correct

> approach to determine whether a patent claim has the utility required. At the same time, the Supreme Court reaffirmed the utility requirement in unequivocal terms and directed that utility be determined as follows:
>
> > (a) First, the court must identify the subject matter of the invention as claimed in the patent;
> >
> > (b) Second, the court asks whether the subject matter is useful. In this regard, "useful" does not mean that "any use will do" - it means that the subject matter works as a "solution to a practical problem", is "capable of an actual relevant use...related to the nature of the subject-matter", and "carries out some useful objective and is not merely a laboratory curiosity whose only possible claim to utility is as a starting material for further research."
>
> 16. The Supreme Court also reaffirmed that the utility as construed must be established by either demonstration or sound prediction as of the filing date of the patent.

[335] 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).

[336] 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.

[337] *AstraZeneca* states that "utility will differ based on the subject-matter of the invention as identified by claims construction" at para 53. 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.

[338] Therefore the Court's utility analysis will proceed on a claim by claim basis, having regard to the construction given each of the asserted claims in the 668 Patent, namely Claims 8, 9, 33, 43 and 44.

[339] **Claims 8 and 9** - I have found that subject matter of Claims 8 and 9 are to the novel crystalline Form I ODV succinate as characterized by its XRPD and endotherm. These claims to the Form I crystal form in my view cover distinct subject matter over the claims of the 668 Patent directed more generally to the novel salt ODV succinate, as the 668 Patent confirms, "[E]ach polymorph forms another aspect of the invention." In this regard, Apotex's Dr. Parr agreed this statement in the 668 Patent means "an aspect of the invention in addition to the invention of the novel salt."

[340] Pfizer says that the usefulness, the utility, of Claims and 9 is its usefulness as a stable, solid state form of ODV succinate. I agree. I also agree that this use is directly related to the subject matter of Claims 8 and 9. Stability (*i.e.*, the tendency not to change to other forms) is an important property for a new crystal form and there is ample evidence that stability was required for this pharmaceutical development.

[341] Apotex disagrees saying that stability is one of the physical properties of the drug (e.g., mass, colour, melting point, stability, etc.), and that utility it is what the drug can do as a practical matter (i.e, treat disease) and not its properties. I disagree: in my respectful view a drug that is not stable across the manufacturing, distribution and storage processes cannot readily be

seen as useful, rather in my view the reverse. I am not persuaded by Apotex's arguments on this point particularly because it is the solid state stability of Form I that makes it possible to use Form I ODV succinate in formulation *i.e.*, as a drug. Both Apotex's Drs. Bastin and Parr agreed stability would be important and a factor. Moreover, Apotex's NOA stated that studies would need to be conducted "to confirm that the solid form of the drug was a sufficiently stable for use in a drug product." The search for a stable form of ODV succinate was a very important motivator lying behind the work done in regard to Wyeth's salt screening, and the polymorph and crystal research undertaken by the specialists at SSC1. While Apotex argues that the stability Pfizer asserts is only the stability of ODV-S Form I (ground), Pfizer correctly observes that this argument is of no moment for the purposes of the *AstraZeneca* utility analysis because even if the claim were limited to "ground" Form I, which I have held is not the case, it was still shown to be useful.

[342] I am satisfied that the solid state stability of Form I ODV succinate, the subject matter of Claims 8 and 9, is subject-matter that is useful - is it capable of a practical purpose (*i.e.* an actual result): it makes it possible to use Form I ODV succinate in formulation *i.e.*, as a drug.

[343] In my respectful view, the stability of Form I was demonstrated. Form I was shown to be stable at room temperature and up to 105ºC, and physically stable from 5% to 95% relative humidity. [redacted] This was the evidence of Dr. Park from her work at SSCI which I accepted at paras 131, 133 and 140 above. Apotex's expert, Dr. Parr admitted that physical stability "was demonstrated

for Form I (ground) ODV succinate." Indeed, Dr. Parr deposed: "If the property of physical stability (*i.e.*, physically stable up to 105 °C and from 5-95% relative humidity) forms part of the promised utility associated with claims 8 and 9, I agree with Drs. Myerson (at his paras 306 to 308) and Atwood (at his paras 269 to 271) that this property was demonstrated for Form I (ground) ODY succinate." Given my finding re stability, the parties agree on demonstration in this respect.

[344] Pfizer also argued that the practical usefulness of the drug as a stable solid form is alone sufficient utility under *AstraZeneca* in this context, and I agree.

[345] Therefore Claims 8 and 9 have demonstrated utility.

[346] **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.

[347] Claim 43, as it depends on Claims 8 or 9, 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.

[348] 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).

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

[349] **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. 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, utility associated with Claim 33 was demonstrated.

[350] 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 it was known 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, as just noted Form I ODV succinate was shown to be capable of getting into the bloodstream at therapeutically effective concentrations.

[351] 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.

[352] **Claims 43 and 44** - In my view the inventors demonstrated at the relevant time that sustained release formulations of ODV succinate (specifically, Form I ODV succinate) that induced the requisite blood plasma level led to an overall reduction in side effects as compared with immediate release formulations.

[353] In my view this use is a practical result related to the subject matter of Claims 43 and 44, which cover sustained release formulations. These formulations are intended to release a drug more slowly in order to reduce blood concentrations and therefore side effects.

B. Conclusion on inutility

[354] I am satisfied on a balance of probabilities that Apotex’s allegations of inutility are not justified.

6. Overpromising in relation to subsection 27(3) of the *Patent Act*

[355] In its post-hearing submissions directed to the Supreme Court of Canada's decision in *AstraZeneca*, Apotex quite expectedly made submissions on the issue of utility. I say expectedly because *AstraZeneca* changed the law in Canada on the Promise Doctrine in the utility analysis. As noted previously, Apotex also made submissions to the effect that *AstraZeneca* altered the law of obviousness, a proposition I did not accept. In addition, Apotex submitted that the 668 Patent "overpromises" in violation of the requirements of subsection 27(3) of the *Patent Act*, such that the Patent is invalid.

[356] To this end, Apotex argued:

> 31. Apotex's alleged and provided evidence to establish that the 668 Patent overpromised. In particular, Apotex alleged that the 668 patent promised (1) high and improved solubility, permeability, and bioavailability when compared with ODV free base and ODV fumarate; (2) the oral administration of ODV-S results in a lower incidence of side effects compared to the administration of venlafaxine, ODV free base and salts of ODV other than ODV-S; and (3) when ODV-S is administered from a sustained release oral dosage form, it results in a lower incidence of side effects relative to the oral administration of venlafaxine, ODV free base, and salts of ODV other than sustained release formulations of ODV-S. Apotex established that these promises were not demonstrated or soundly predicted as of the filing date of the 668 patent.
>
> 32. Pfizer did not dispute that these promises were made, but rather asserted that not all of these promises ought to constitute the utility of each of the claims. For example, Pfizer's position was that the promises of improvements in side effects ((2) and (3) above) ought be read to inform the utility of claims other than claims 8, 9 and 33.

> 33. As noted above, in AstraZeneca, the Supreme Court directed that overpromising violates the requires of subsection 27(3) of the Patent Act. An invention is subject matter that has demonstrated utility as of the filing date, or subject that matter that constitutes a sound prediction as of the filing date. The statements in the 668 patent to the effect that the compounds of the patent have the utilities (1)-(3) above were thus not 'correct and full' descriptions of the invention but rather were overpromises. As such, they ought to invalidate the 668 patent as a whole.

[357] I agree that the Supreme Court of Canada in *AstraZeneca* declared overpromising to be a "a mischief". However, instead of addressing overpromising within the law of utility, as the Promise Doctrine had done, the Supreme Court directed at para 46 that "the scheme of the [*Patent*] *Act* treats the overpromising in multiple ways", including reference to subsection 27(3) of the *Patent Act*. Subsection 27(3) provides:

Specification	**Mémoire descriptive**
(3) The specification of an invention must	Le mémoire descriptif doit :
(a) correctly and fully describe the invention and its operation or use as contemplated by the inventor;	**a)** décrire d'une façon exacte et complète l'invention et son application ou exploitation, telles que les a conçues son inventeur;
(b) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is most closely connected, to make, construct, compound or use it;	**b)** exposer clairement les diverses phases d'un procédé, ou le mode de construction, de confection, de composition ou d'utilisation d'une machine, d'un objet manufacturé ou d'un composé de matières, dans des termes complets, clairs, concis et exacts qui permettent à toute personne versée dans l'art ou la science dont relève l'invention, ou dans l'art ou la science qui s'en rapproche le plus, de

	confectionner, construire, composer ou utiliser l'invention;
(c) in the case of a machine, explain the principle of the machine and the best mode in which the inventor has contemplated the application of that principle; and	**c)** s'il s'agit d'une machine, en expliquer clairement le principe et la meilleure manière dont son inventeur en a conçu l'application;
(d) in the case of a process, explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions.	**d)** s'il s'agit d'un procédé, expliquer la suite nécessaire, le cas échéant, des diverses phases du procédé, de façon à distinguer l'invention en cause d'autres inventions.

[358] Apotex raises an entirely new argument in this connection. It made no reference to overpromising in its memorandum of fact and law. Nor did it refer to overpromising in any of the outlines of argument filed at the hearing. Nor was overpromising discussed by Apotex at the hearing. And while Apotex did refer to subsection 27(3) of the *Patent Act* in its memorandum, it made but a single reference and that was in connection with insufficiency and overbreadth; Apotex subsequently withdrew both those arguments.

[359] While I do not fault Apotex for raising its "overpromise" doctrine given the invitation to make additional comments on *AstraZeneca,* I note Apotex did not ask to raise "overpromising" in its letter of July 4, 2017, in which it requested a broadening of the scope of post hearing submissions: it only asked to raise anticipation and obviousness. Thus, while Apotex raised obviousness in its post-hearing filings, it said nothing about anticipation; instead it raised the new issue of "overpromising".

[360] I also observe that the alleged overpromises resemble the promise arguments advanced by Apotex, which are no longer valid having regard to *AstraZeneca*. If the Supreme Court intended to say, in effect, that the Promise Doctrine was not good law in terms of utility under s 2, but was good law in terms of patent specifications under subsection 27(3) it could have done so; it did not.

[361] Pfizer opposes Apotex's submissions on overpromising. It puts its argument this way:

> 4. Apotex's position in both this case and in *AstraZeneca* was that s. 2 of the *Act* requires a patentee to demonstrate or predict every plausible benefit mentioned in the patent's specification. The Supreme Court described that position and the Promise Doctrine as "unsound," "excessively onerous," "incongruent with … the scheme of the [*Act*]" and "not good law." Undeterred by this strong language, Apotex now suggests that this requirement was correct all along and should still be applied, and that what the Supreme Court corrected was the relevant section of the *Act* (s. 27(3) instead of s. 2). This Court should not accept Apotex's opportunistic invitation to rewrite long-established disclosure principles – and the *Act* itself – on the basis of an obiter comment of the Supreme Court.
>
> 5. The Supreme Court did not direct that "overpromising violates the require[ments] of subsection 27(3)." Read purposively, the Court was referring to those extraordinary circumstances in which the statements in a patent prevent a skilled reader from understanding "the nature of the invention" or "how it is put into operation." These have always been (and remain) the core requirements of s. 27(3), as the Supreme Court has recently re-affirmed in *Teva v. Pfizer*.
>
> 6. Section 27(3) represents the patent bargain. It exists to ensure that "when the period of monopoly has expired the public will be able … to make the same successful use of the invention as the inventor could at the time of his application." The promise doctrine was eliminated, among other reasons, because it discourages rather than encourages disclosure. As the Supreme Court said, "[t]o invalidate a patent solely on the basis of an

> unintentional overstatement of even a single use will discourage a patentee from disclosing fully, whereas such disclosure is to the advantage of the public."

[362] The Supreme Court in *AstraZeneca* stated:

> [45] Supporters of the doctrine assert that the consequences of the Promise Doctrine play a key role in ensuring patentees do not "overpromise" in their patent applications. That is, a patentee will be dissuaded from stating the invention can be used for things that are not sufficiently established at the time of filing if doing so would risk invalidating the entire patent. The utility requirement should not be interpreted, however, as the Federal Courts have done, to address such concerns. Nonetheless, overpromising is a mischief.
>
> [46] The scheme of the Act treats the mischief of overpromising in multiple ways. There are consequences for failing to properly disclose an invention by claiming, for instance, that you have invented more than you have. 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). An overly broad claim may be declared invalid; however, under the operation of s. 58 of the *Patent Act*, remaining valid claims can be given effect. As well, this mischief may result in a patent being void under s. 53 of the Act, where overpromising in a specification amounts to an omission or addition that is "willfully made for the purpose of misleading".

[363] It seems to me that Pfizer is correct. I am unable to see a rationale for the argument that the Supreme Court of Canada removed the Promise Doctrine from the utility analysis yet simultaneously required it to be considered, in the manner Apotex proposes, in the specification analysis. If that was the case, a major underlying problem identified by the Supreme Court itself would remain, namely that "a patentee will be dissuaded from stating the invention can be used

for things that are not sufficiently established at the time of filing if doing so would risk invalidating the entire patent." See *AstraZeneca* para 45.

[364] Not only would this underlying problem persist, but I do not see anything in *AstraZeneca* to the effect that the Supreme Court intended to overrule itself on the focus of subsection 27(3)'s disclosure requirements, which the Supreme Court itself had recently outlined in *Teva Canada Ltd v Pfizer Canada Inc*, [2012] 3 SCR 625 [*Teva*]:

> [49] In *Consolboard*, this Court reviewed the Act's disclosure requirements, which at that time were found in s.36. Although there are variations in wording between that section and the current s. 27(3), the substance of the disclosure requirements has remained the same.
>
> [50] Dickson J. discussed what the specification must contain in order to meet the disclosure requirements. He stated clearly that the nature of the invention must be disclosed and that the entire specification, including the claims, must be considered in determining the nature of the invention and whether disclosure was sufficient:
>
> > In essence, what is called for in the specification (which includes both the "disclosure", *i.e.* the descriptive portion of the patent application, and the "claims") is a description of the invention and the method of producing or constructing it, coupled with a claim or claims which state those novel features in which the applicant wants an exclusive right. <u>The specifications must define the precise and exact extent of the exclusive property and privilege claimed.</u>
> >
> > Section 36(1) seeks an answer to the questions: "What is your invention? How does it work?" <u>With respect to each question the description must be correct and full</u> in order that, as Thorson P. said in *Minerals Separation North American Corporation v. Noranda Mines, Limited* [[1947] Ex. C.R. 306]:

> … when the period of monopoly has expired the public will be able, having only the specification, to make the same successful use of the invention as the inventor could at the time of his application. [at p. 316]

> We must look to the whole of the disclosure and the claims to ascertain the nature of the invention and methods of its performance, … being neither benevolent nor harsh, but rather seeking a construction which is reasonable and fair to both patentee and public. There is no occasion for being too astute or technical in the matter of objections to either title or specification for, as Duff C.J.C. said, giving the judgment of the Court in *Western Electric Company, Incorporated, and Northern Electric Company v. Baldwin International Radio of Canada* [[1934] S.C.R. 570], at p. 574, "where the language of the specification, upon a reasonable view of it, can be so read as to afford the inventor protection for that which he has actually in good faith invented, the court, as a rule, will endeavour to give effect to that construction". Sir George Jessel spoke to like effect at a much earlier date in *Hinks & Son v. Safety Lighting Company* [(1876), 4 Ch. D. 607]. He said the patent should be approached "with a judicial anxiety to support a really useful invention".
>
> …
>
> In my view it is a well established principle that a patent specification is addressed, not to the public generally, but to persons skilled in the particular art. I am further of the opinion that s. 36(1) does not impose upon a patentee the obligation of establishing the utility of the invention. [Emphasis added; citation omitted; pp. 520-21.]

Since Consolboard, the Court has constantly applied the principles stated by Dickson J., which is a testament to the soundness of his reasoning: see, e.g., Monsanto Canada Inc. v. Schmeiser, 2004 SCC 34, [2004] 1 S.C.R. 902, at para. 18; Whirlpool Corp. v. Camco Inc., 2000 SCC 67, [2000] 2 S.C.R. 1067, at para. 52;

> Pioneer Hi-Bred Ltd. v. Canada (Commissioner of Patents), [1989] 1 S.C.R. 1623 ("Pioneer Hi-Bred"), at p. 1636.
>
> [51] In *Pioneer Hi-Bred*, the Court referred to *Consolboard* in discussing the Act's disclosure requirements once again. Lamer J. (as he then was), writing for the Court, described those requirements as follows:
>
> > In summary, the *Patent Act* requires that the applicant file a specification including disclosure and claims (*Consolboard Inc., supra*, at p. 520). Canadian courts have stated in a number of cases the test to be applied in determining whether disclosure is complete. The applicant must disclose everything that is essential for the invention to function properly. To be complete, it must meet two conditions: it must describe the invention and define the way it is produced or built …. The applicant must define the nature of the invention and describe how it is put into operation. A failure to meet the first condition would invalidate the application for ambiguity, while a failure to meet the second invalidates it for insufficiency. The description must be such as to enable a person skilled in the art or the field of the invention to produce it using only the instructions contained in the disclosure . . . and once the monopoly period is over, to use the invention as successfully as the inventor could at the time of his application (*Minerals Separation, supra*, at p. 316). [Emphasis added; citations omitted; pp. 1637-38.]
>
> [52] In *Consolboard* and in *Pioneer Hi-Bred*, the Court correctly analysed the disclosure requirements set out in s. 27(3) of the Act. The reasoning in those cases should be reaffirmed and applied in the case at bar.
>
> [Emphasis in original.]

[365] I see nothing in *AstraZeneca* that alters what I take from the foregoing namely that the specifications analysis under subsection 27(3) requires the patentee to define the precise and exact extent of the exclusive property and privilege claimed. In addition, nothing in *AstraZeneca*

departs from the proposition that under subsection 27(3), "the applicant must disclose everything that is essential for the invention to function properly. To be complete, it must meet two conditions: it must describe the invention and define the way it is produced or built …. The applicant must define the nature of the invention and describe how it is put into operation. A failure to meet the first condition would invalidate the application for ambiguity, while a failure to meet the second invalidates it for insufficiency." See *Teva* at para 51 citing to *Pioneer Hi-Bred Ltd v Canada (Commissioner of Patents)*, [1989] 1 SCR 1623, pp. 1637-38.

[366] In the circumstances I do not agree with Apotex's allegations on overpromising, and therefore find on a balance of probabilities that they are not justified.

7. Anticipation

[367] Apotex points to the following summary of the law of anticipation set out in *Gilead Sciences Inc v Canada (Health)*, 2016 FC 857:

> [71] The definition of "invention" in section 2 of the *Patent Act* requires that it be "new", which engages the law of anticipation referred to in s. 28.2 of the *Patent Act* each of which are set out below:

2 In this Act, except as otherwise provided,	2 Sauf disposition contraire, les définitions qui suivent s'appliquent à la présente loi.
(…)	(…)
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	*invention* Toute réalisation, tout procédé, toute machine, fabrication ou composition de matières, ainsi que tout perfectionnement de l'un d'eux, présentant le caractère

or composition of matter; (invention)	de la nouveauté et de l'utilité. (invention)
28.2 (1) The subject-matter defined by a claim in an application for a patent in Canada (the "pending application") must not have been disclosed	28.2 (1) L'objet que définit la revendication d'une demande de brevet ne doit pas :
(a) 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 subject-matter became available to the public in Canada or elsewhere; (…)	a) plus d'un an avant la date de dépôt de celle-ci, avoir fait, de la part du demandeur ou d'un tiers ayant obtenu de lui l'information à cet égard de façon directe ou autrement, l'objet d'une communication qui l'a rendu accessible au public au Canada ou ailleurs; (…)
[Emphasis added.]	[Soulignement ajouté.]

[72] The Supreme Court of Canada in *Apotex Inc v Sanofi Synthelabo Canada Inc*, 2008 SCC 61 at paras 18-37 [*Sanofi*] held that anticipation consists in one publicly available document disclosing the content of the patent at issue, such that the patent would infringe the prior disclosure when made, and secondly, that the prior disclosure must enable the Skilled Person to make the invention as claimed:

> [20] In his reasons after referring to s. 27(1) of the Act, the applications judge defined anticipation as meaning "that the exact invention had already been made and publicly disclosed" (para. 55). Shore J. cited this Court's decision in *Free World Trust v. Electro Sante Inc.*, [2000] 2 S.C.R. 1024, 2000 SCC 66, at para. 26, which approved of the test for anticipation described in *Beloit Canada Ltd. v. Valmet OY* (1986), 8 C.P.R. (3d) 289 (F.C.A.), at p. 297:
>
> > One must, in effect, be able to look at a prior, single publication and find in it all the information which, for practical purposes, is needed to produce the claimed invention without the exercise of any inventive skill. *The prior publication must contain so clear*

> *a direction that a skilled person reading and following it would in every case and without possibility of error be led to the claimed invention*. [Emphasis added by the applications judge.]

[21] The applications judge noted that the English Court of Appeal stated in *General Tire & Rubber Co. v. Firestone Tyre & Rubber Co.*, [1972] R.P.C. 457, at p. 486:

> *If, on the other hand, the prior publication contains a direction which is capable of being carried out in a manner which would infringe the patentee's claim, but would be at least as likely to be carried out in a way which would not do so, the patentee's claim will not have been anticipated, although it may fail on the ground of obviousness*. To anticipate the patentee's claim the prior publication must contain clear and unmistakable directions to do what the patentee claims to have invented [Emphasis added by the applications judge.]

He then noted that in *Free World*, at para. 26, this Court approved the following statement from *General Tire*:

> A signpost, however clear, upon the road to the patentee's invention will not suffice. The prior inventor must be clearly shown to have planted his flag at the precise destination before the patentee. [p. 486]

[22] The law of anticipation as explained in Beloit and General Tire has been accepted in Canada without reservation: see Free World, at para. 26. In his application of the law to the facts, there is no doubt that Shore J. was using the test as set out in Beloit when he stated, at para. 57:

> Based on the law, the question before the Court is whether a person skilled in the art was given such a clear direction that, by

> reading and following the ‘875 patent (or its U.S. or French equivalents) would in every case and without possibility of error make a compound or pharmaceutical composition within the claims of the ‘777 patent (e.g. the bisulfate salt of clopidogrel).

(c) Recent United Kingdom Jurisprudence

> [23] For the reasons that follow, and in light of recent jurisprudence, I am of the respectful opinion that the applications judge overstated the stringency of the test for anticipation that the “exact invention” has already been made and publicly disclosed.
>
> [24] In the 2005 decision of the House of Lords in *Synthon*, Lord Hoffmann has brought some further clarity to the law of anticipation as understood since *General Tire*. His reference at para. 20 to the “unquestionable authority” of Lord Westbury in *Hills v. Evans* (1862), 31 L.J. Ch. (N.S.) 457, at p. 463, makes it plain that his analysis does not depend on any change on English law flowing from the enactment of the *Patents Act 1977* (U.K.), 1977, c. 37, or the U.K.’s adoption of the *Convention on the Grant of European Patents*, 1065 U.N.T.S. 199 (entered into force October 7, 1977). He distinguishes between two requirements for anticipation that were not theretofore expressly considered separately, prior disclosure and enablement.
>
> [25] [In the 2005 decision of the House of Lords in *Synthon*, Lord Hoffmann] explains that the requirement of prior disclosure means that the prior patent must disclose subject matter which, if performed, would necessarily result in infringement of that patent, and states, at para. 22:
>
> > If I may summarise the effect of these two well- known statements [from *General Tire and Hills v. Evans*], the matter relied upon as prior art must disclose subject matter which, if performed, would necessarily result in an infringement of the patent... It follows that,

> whether or not it would be apparent to anyone at the time, whenever subject matter described in the prior disclosure is capable of being performed and is such that, if performed, it must result in the patent being infringed, the disclosure condition is satisfied.

When considering the role of the person skilled in the art in respect of disclosure, the skilled person is "taken to be trying to understand what the author of the description [in the prior patent] meant" (para. 32). At this stage, there is no room for trial and error or experimentation by the skilled person. He is simply reading the prior patent for the purposes of understanding it.

[26] If the disclosure requirement is satisfied, the second requirement to prove anticipation is "enablement" which means that the person skilled in the art would have been able to perform the invention (para. 26).

…

(1) Disclosure

[74] As stated in *Sanofi*, in order for there to be disclosure of the 619 Patent, the EP 214 application must have disclosed all the information that is needed for the Skilled Person, without inventive skill, to make the claimed invention, where the claimed invention necessarily infringes the prior disclosure. And, as stated in para 25 in *Sanofi*, "when considering the role of the person skilled in the art in respect of disclosure, the skilled person is 'taken to be trying to understand what the author of the description [in the prior patent] meant' […]. At this stage, there is no room for trial and error or experimentation by the skilled person. He is simply reading the prior patent for the purposes of understanding it".

[368] Apotex referred the Court to and I accept what Justice Hughes said regarding the legal and evidentiary obligations of first and second persons in *Allergan Inc v Canada (Health)*, 2012 FC 767 [*Allergan*]:

> **ISSUE #1: Who bears the burden?**
>
> [42] As to the allegations of invalidity, the *Patent Act*, RSC 1985, P-4, section 43(2) affords a presumption of validity; however, once a second person, here Apotex, puts in some evidence as to invalidity, the Court must determine the matter on the usual civil burden; namely, balance of probabilities. I repeat what I wrote in *GlaxoSmithKline Inc v Pharmascience Inc*, 2011 FC 239 at paras 43 and 44:
>
> > *43 O'Reilly J of this Court has summarized the question of burden of proof where the issue is invalidity in Pfizer Canada Inc. v. Apotex Inc., 2007 FC 26, 59 CPR(4th) 183 (aff'd 2007 FCA 195, leave to appeal refused [2007] SCCANo. 371) at paragraphs 9 and 12:*
> >
> > > *9 In my view, the burden on a respondent under the Regulations is an "evidential burden" -- a burden merely to adduce evidence of invalidity. Once it has discharged this burden, the presumption of validity dissolves and the Court must then determine whether the applicant has discharged its legal burden of proof. I believe this is what is meant in those cases where the Court has stated that the respondent must put its allegations "into play". It must present sufficient evidence to give its allegations of invalidity an air of reality.*
> > >
> > > *...*
> > >
> > > *12 To summarize, Pfizer bears the legal burden of proving on a balance of probabilities that Apotex's allegations of invalidity are unjustified. Apotex merely has an evidentiary burden to put its case "into*

> *play" by presenting sufficient evidence to give its allegations of invalidity an air of reality. If it meets that burden, then it has rebuttedthe presumption of validity. I must then determine whether Pfizer has established that Apotex's allegations of invalidity are unjustified. If Apotex does not meet its evidential burden, then Pfizer can simply rely on the presumption of validity to obtain its prohibition order.*

44 In Pfizer Canada Inc. v. Canada (Minister of Health), 2008 FC 11, 69 C.P.R. (4th) 191, I said in respect of the same thing at paragraph 32:

> *32 I do not view the reasoning of the two panels of the Federal Court of Appeal to be in substantial disagreement. Justice Mosley of this Court reconciled these decisions in his Reasons in Pfizer Canada Inc. v. Apotex Inc., [2007] F.C.J. No. 1271, 2007 FC 971 at paragraphs 44 to 51. What is required, when issues of validity of a patent are raised:*
>
> > *1. The second person, in its Notice of Allegation may raise one or more grounds for alleging invalidity;*
> >
> > *2. The first person may in its Notice of Application filed with the Court join issue on any one or more of those grounds;*
> >
> > *3. The second person may lead evidence in the Court proceeding to support the grounds upon which issue has been joined;*
> >
> > *4. The first person may, at its peril, rely simply upon the presumption of validity afforded by the Patent Act or, more prudently, adduce its own evidence as to the grounds of invalidity put in issue.*
> >
> > *5. The Court will weigh the evidence; if the first person relies only on the*

> *presumption, the Court will nonetheless weigh the strength of the evidence led by the second person. If that evidence is weak or irrelevant the presumption will prevail. If both parties lead evidence, the Court will weigh all the evidence and determine the matter on the usual civil balance.*
>
> *6. If the evidence weighed in step 5 is evenly balanced (a rare event), the Applicant (first person) will have failed to prove that the allegation of invalidity is not justified and will not be entitled to the Order of prohibition that it seeks.*

[Emphasis added.]

[369] The issue of anticipation came before this Court in an unusual manner.

[370] Apotex raised anticipation in its NOA. Pfizer, as the Applicant in this proceeding, provided the Court with evidence of experts who had been instructed on anticipation (Drs. Atwood and Myerson). However, Pfizer did not address anticipation in its memorandum of fact and law. Instead, Pfizer took the position (in a footnote in its memorandum) that anticipation was not before the Court because Apotex had not filed evidence concerning the anticipation of any claim in the material it file responding to this application. The footnote added that Pfizer reserved the right to make submissions in response should Apotex "pursue any additional issues at the hearing."

[371] At the hearing, Pfizer maintained its position that anticipation was not before the Court because Apotex had not dealt with the issue of anticipation in the evidence it filed for the

hearing. Pfizer also argued that the evidence Apotex relied on was of no value because Apotex's experts had not been instructed in the law of anticipation, or in terms of either disclosure or enablement, key concepts related to anticipation.

[372] The resolution of this issue turns on the evidence: *Abbott Laboratories v Apotex Inc*, 2007 FCA 153 at paras 9 and 10. In terms of the evidence before this Court, Apotex relied on the affidavit evidence of Dr. Steed and Dr. Bastin to give its allegation of anticipation an air of reality sufficient to displace the statutory presumption of validity set out in s 43(2) of the *Patent Act*.

[373] However I am unable to accept this evidence for several reasons. First, as Pfizer correctly pointed out, neither Drs. Bastin nor Steed were instructed on the law of anticipation, and neither was instructed on either disclosure or enablement. I am unable to see how the Court may confidently accept what is stated by a scientific expert witness when he or she has no understanding of the legal meaning of the words or concepts at issue.

[374] Second, the fact is that the evidence of both Dr. Steed and Dr. Bastin was not tendered in respect of anticipation; it was tendered in connection with the issues of obviousness and obvious to try.

[375] The evidence of Dr. Steed that Apotex asks the Court to rely upon was tendered under the heading: X. "Sixth mandate -Differences between inventive concepts of the claims of the 668

Patent and the state of the art and common general knowledge", subheading b. "The state of the art and common general knowledge as of February 12, 2001", sub-subheading 2(ii) "Patents disclosing different forms of ODV and formulations of ODV", and subheading d. "Was inventive ingenuity required to overcome this difference."

[376] The evidence of Dr. Bastin that Apotex asks the Court to rely on regarding anticipation, was likewise not given in respect of anticipation (like Dr. Steed, he nowhere uses the word), but was instead tendered under the heading: VI. "Would the skilled person have required inventive ingenuity to arrive at the inventive concept of claims 1, 2, 4 to 9, 20, 21, 23 to 28, and 31 to 33 of the 668 Patent?", subheading 2. "The common general knowledge of the skilled person and the state of the art", subsub heading I. "ODV, its salts, dosage forms, and uses", and X. "The affidavits of Drs. Myerson, Atwood, Polli and Blier", subheading 4. "The opinion that compositions of ODV succinate and their preparation would not be obvious", and subheading 5. "The opinion that the use of ODV succinate was not obvious".

[377] Thus, their evidence was not tendered in respect of anticipation but in connection with the issue of obvious to try and obviousness. This is underscored by the fact that neither Drs. Bastin nor Steed use the word "anticipation" anywhere in their evidence.

[378] In this connection, I note that Dr. Bastin uses the words "disclose" and "enable" in his affidavit; likewise Dr. Steed also uses the word "disclosed". However, I was given no reason to accept their evidence as useful to the Court given that neither was instructed in respect of

anticipation, disclosure or enablement; on this basis alone what they said is not acceptable to assist the Court in its anticipation inquiry.

[379] Use of such words in parts of affidavits directed to obviousness was also insufficient to put Pfizer on notice that Apotex was going to use that evidence in support of its allegation of anticipation. Apotex's failure to file proper evidence on anticipation led Pfizer to reasonably conclude, at the time it filed its memorandum, that it did not need to deal with anticipation. Therefore Pfizer was not in breach of Rule 70(1)(c) of the *Rules of the Federal Courts*, SOR/98-106 when it filed its memorandum.

[380] Apotex says it may rely on this alleged evidence of anticipation notwithstanding these defects; I disagree for two reasons. First, I am not prepared to accept as of assistance to the Court evidence on the issue of anticipation offered by a witness not instructed on the law of anticipation, a point I have already made. Secondly, in my respectful view, neither party should be allowed to imbed critical evidence on one issue into material filed in relation to another and different issue, and then, after all the evidence including reply affidavits and cross-examinations is complete, rely on the imbedded evidence to attack the patent.

[381] To rule otherwise would not only allow expert evidence in respect of matters where the "expert" has no proper basis on which to give an opinion. It would reward litigation by surprise. It would also encourage the playing of hide-and-seek and guessing games. This is not just a question of headings as Apotex argued, but a matter of basic fairness. All parties to a NOC, not

to mention the Court, are entitled to proper pleadings including affidavits to eliminate such conduct so as to best ensure efficient determination of the issues.

[382] That said, I agree with Apotex that Pfizer may not split its case by declining to deal with the merits of an issue in its memorandum and then dealing with that issue in oral reply at the end of the hearing. Here, Pfizer argued the absence of properly instructed expert evidence in its memorandum. In oral argument in chief Pfizer again pointed to its own expert evidence on the issue of anticipation. Apotex in response took the Court through its alleged evidence on anticipation, taking the position it had thereby put anticipation into play and was entitled to succeed given Pfizer's position. In reply, Pfizer's counsel dealt with Apotex's submissions and then as I understood it, attempted to engage the Court on the merits of an anticipation argument, to which Apotex objected. I ruled I would hear Pfizer's argument, reserving on what I would do with it. In the circumstances, I will not rely on Pfizer's reply argument on the merits of anticipation because to do so would allow case splitting.

[383] In my view, once Apotex filed its memorandum dealing with anticipation, which made it plain that anticipation was still in issue, Pfizer could no longer proceed on the assumption that anticipation was not in issue. That anticipation was still in issue was further confirmed in a joint letter to the Court from counsel dated June 9, 2017, the Friday before the hearing which started on the 12th. Pfizer could have sought leave to file a supplementary memorandum after it received Apotex's responding memo, or taken other steps, but did not. I am not saying that such permission would have been granted or dismissed because the point was not argued.

[384] In the end, I am asked by Apotex to rely on Justice de Montigny's [as he then was] decision in *Eli Lilly Canada Inc v Mylan Pharmaceuticals*, 2015 FC 125 at para 79, and accept the evidence of Drs. Steed and Bastin, as a substitute for properly instructed and acceptable expert evidence on anticipation notwithstanding the other circumstances of this case.

[385] In the particular circumstances of this case, and for the reasons already given, I am not prepared to do so.

[386] Apotex also relied on the allegations of anticipation it made in its NOA as evidence to displace the statutory presumption. However, and with respect, while allegations of non-infringement in a NOA are presumed to be true: *Merck Frosst Canada Inc v Canada (Minister of National Health and Welfare)*, [1994] FCJ No 662 at paras 23-24 (FCA) (QL), leave to appeal to SCC refused, [1994] SCCA No 330 (SCC) (QL)), I have no authority for the proposition that allegations of anticipation in a NOA benefit from the same presumption or are "evidence" for the purposes of the factors set out above in the *Allergan* decision.

[387] Apotex also relied on the WO 851 Patent in support of its allegation of anticipation. I have already discussed the WO 851 Patent, and found that as prior art it did not disclose the Form I ODV succinate at issue in Claims 8 and 9. Since Claims 33, 43 and 44 depend on claims 8 and 9, the WO 851 Patent does not assist Apotex on the issue of anticipation.

[388] Therefore as I see it, and with respect, this situation gives rise to the 5th factor in the passage of Justice Hughes in *Pfizer Canada Inc v Canada (Minister of Health),* 2008 FC 11 at para 32, cited in *Allergan*, above, which states that: "[T]he Court will weigh the evidence; if the first person relies only on the presumption, the Court will nonetheless weigh the strength of the evidence led by the second person. If that evidence is weak or irrelevant the presumption will prevail."

[389] Pfizer relies on the presumption. Because I have not accepted the evidence given by the second person (Apotex), it must be considered weak in terms of that 5th factor. Therefore the presumption of validity will and does prevail.

[390] I find on a balance of probabilities that Apotex's allegation in respect of anticipation is not justified.

8. Double patenting

[391] It is common ground that the *Patent Act* only entitles an inventor to a single patent for each invention. Thus, a second patent will fail for double patenting if its claims are (i) "coterminous" with the claims of a prior patent, sometimes called "same invention" double patenting, or, (ii) if its claims lack ingenuity over the claims of an earlier patent (*i.e.*, the claims are not "patentably distinct"), sometimes described as "obviousness" double patenting.

[392] The Supreme Court of Canada said in *Whirlpool Corp v Camco Inc,* 2000 SCC 67:

63 The prohibition against double patenting relates back to the "evergreen" problem mentioned at the outset. The inventor is only entitled to "a" patent for each invention: *Patent Act*, s. 36(1). If a subsequent patent issues with identical claims, there is an improper extension of the monopoly. It is clear that the prohibition against double patenting involves a comparison of the claims rather than the disclosure, because it is the claims that define the monopoly. The question is how "identical" the claims must be in the subsequent patent to justify invalidation.

64 The Federal Court of Appeal has adopted the test that the claims must be "identical or conterminous": *Beecham Canada Ltd. v. Procter & Gamble Co.* (1982), 61 C.P.R. (2d) 1, at p. 22. This verbal formulation derives from an editorial comment by Dr. H. G. Fox, Q.C., on *Lovell Manufacturing Co. v. Beatty Bros. Ltd.*, reported at (1962), 23 Fox Pat. C. 112, at pp. 116-17:

> Letters patent are not granted at pleasure, but for a term of years and the grant of a second patent with respect to the same subject-matter would be void under this statute [6 Henry VIII, c. 15, 1514] and by the Statute of Monopolies, as well as at common law and by the terms of section 28(1)(b) of the Canadian Patent Act. But for this purpose the subject-matter of the two grants must be identical. A subsequent claim cannot be invalidated on the ground of prior claiming unless the two claims are precisely conterminous.

65 This branch of the prohibition on double patenting is sometimes called "same invention" double patenting. Given the claims construction adopted by the trial judge it cannot be said that the subject matter of the '734 patent is the same or that the claims are "identical or conterminous" with those of the '803 patent.

66 There is, however, a second branch of the prohibition which is sometimes called "obviousness" double patenting. This is a more flexible and less literal test that prohibits the issuance of a second patent with claims that are not "patentably distinct" from those of the earlier patent. In *Commissioner of Patents v. Farbwerke Hoechst Aktiengesellschaft Vormals Meister Lucius & Bruning*, [1964] S.C.R. 49, the issue was whether Farbwerke Hoechst could obtain a patent for a medicine that was a diluted version of a medicine for which it had already obtained a patent. The claims were neither identical nor conterminous. Judson J.

nevertheless held the subsequent patent to be invalid, explaining at p. 53:

> A person is entitled to a patent for a new, useful and inventive medicinal substance but to dilute that new substance once its medical uses are established does not result in further invention. The diluted and undiluted substance are but two aspects of exactly the same invention. In this case, the addition of an inert carrier, which is a common expedient to increase bulk, and so facilitate measurement and administration, is nothing more than dilution and does not result in a further invention over and above that of the medicinal itself. [Emphasis added.]

67 In *Consolboard*, supra, Dickson J. referred to *Farbwerke Hoechst* as "the main authority on double patenting" (p. 536) which stood for the proposition that a second patent could not be justified unless the claims exhibited "novelty or ingenuity" over the first patent:

> Judson J. for the Court said that the second process involved no novelty or ingenuity, and hence the second patent was unwarranted.

68 It is on this second branch of "obviousness" double patenting that the appellants rest their case against all of the claims of the '734 patent except the "continuous drive" claims which they concede to be valid albeit they contest infringement.

[393] The Federal Court of Appeal in *Pharmascience Inc v Sanofi-Aventis Canada Inc*, 2006 FCA 229 [*Pharmascience*] also discussed the two concepts of double patenting:

> 68 The jurisprudence has so far identified two categories of double patenting. In the first category, "same invention patenting", two patents are the same or have an identical or conterminous claim. The second category, "obviousness double patenting", is somewhat broader. In obviousness double patenting, the claims of the patents are not identical or conterminous, but the later patent has claims that are not patentably distinct from the other patent, or involve no novelty or ingenuity.

[394] Recently, Justice Manson of this Court set out the law of double patenting in *Bristol-Myers Squibb Canada v Apotex Inc*, 2017 FC 296:

> B. Double Patenting
>
> (1) Law
>
> [203] Section 36(1) of the *Patent Act* states "[a] patent shall be granted for one invention only but in an action or other proceeding a patent shall not be deemed to be invalid by reason only that it has been granted for more than one invention". The patent bargain is in the interest of both the patentee and the public "only if the patent owner acquires real protection in exchange for disclosure, and the public does not for its part surrender a more extended monopoly than the statutory [20] years from the date of the patent grant" (*Whirlpool Corp v Camco Inc*, 2000 SCC 67 at para 37 [*Whirlpool*]).
>
> [204] Double patenting occurs when two patents are issued to the same inventor, and the subsequent patent has identical claims to the first (*Whirlpool*, above, at para 63). Determining whether double patenting has occurred requires the Court to compare the claims, not the disclosures, of both patents and determine whether the patents are (1) "identical or coterminous"; or (2) obvious, such that the claims of the second patent are "not 'patentably distinct' from those of the earlier patent" (*Whirlpool* at paras 63 to 66).
>
> [205] A second patent cannot be justified unless the claims exhibit novelty or ingenuity over the first patent (*Whirlpool* at para 67).

[395] In its memorandum, Apotex puts its case this way:

> 66. The *Patent Act* only entitles an inventor to a single patent for each invention. A second patent will fail for double patenting if its claims are "coterminous" with the claims of a prior patent, or, if its claims lack ingenuity over the claims of an earlier patent. In the case of obviousness-type double patenting, the question is whether the skilled person reading the first patent together with his or her common general knowledge, would arrive at the claims of the second patent without exercising inventive ingenuity.

> 67. The 540 patent issued on January 10, 2010 and is the corresponding Canadian equivalent to US 186 discussed above. Like the patent, the 540 patent is owned by Wyeth.
>
> 68. Claim 21 of the 540 patent is specifically directed to "ODV or a pharmaceutically acceptable salt thereof'. The skilled person would have understood that ODV-S is included within the scope of this claim. Further, the disclosure of the 540 patent specifies that succinate salts are among the "pharmaceutically acceptable salts" of its compounds. Practising these claims will yield ODV-S Form I. As such, at all material times, claims 8 and 9 of the patent represent double patenting over claim 21 of the 540 patent.

[396] Pfizer in its memorandum said:

> 54. **No Double Patenting over CA 540**. Apotex alleges that claims 8, 9, 33, 43 and 44 of the 668 Patent are invalid for double patenting over claim 21 of the 540 Patent. The 540 Patent discloses a class of chemical compounds which includes ODV. Claim 21 covers ODV or a pharmaceutically acceptable salt thereof. The claim does not mention which, if any, of the possible salts of ODV would be contemplated, and does not mention which solid state forms of those salts would be included. Claim 21 is not a claim to the "same invention" as any of claims 8, 9, 33, 43 or 44, which are claims to new solid-state forms, uses and formulations of a particular salt form of ODV.
>
> 55. For the same reasons addressed above in respect of obviousness, there is no obviousness-type double patenting over claim 21 of the 540 Patent. A skilled person could not know from claim 21 what the properties of any particular salt form of ODV may be. They would not know whether (or how) it could be made as a crystalline solid, what crystalline solids may exist, or whether any particular salt or solid form would have properties amenable to formulation and development (including as a SR formulation). The only salt form of ODV taught by the 540 Patent is the fumarate. No properties (beyond a melting point) of that salt are provided. The patent discloses the possibility that other pharmaceutically acceptable salts of the "compounds of the invention" could exist, but there is no specific indication that the succinate salt of ODV could be formed, would be crystalline or would have any of the properties disclosed in the 668 Patent.

[397] It is not disputed that Claim 21 in the earlier CA 540 Patent, which was owned by a Pfizer company, covers ODV or a pharmaceutically acceptable salt thereof. The claim does not state which, if any, of the possible salts of ODV would be contemplated, and does not mention which solid state forms of those salts would be included. In my view, and as I have construed them, there is no "coterminous" sometimes called "same invention" double patenting involved in Claims 8 or 9 of the 668 Patent in relation to Claim 21 of the CA 540 Patent.

[398] Therefore the issue is whether the 668 Patent lacks ingenuity or, put another way, constitutes obviousness-type double patenting. Thus the question - and on this the parties agree - is whether the Skilled Person reading the relevant claim of the CA 540 Patent (together with his or her common general knowledge) would arrive at the claims of the 668 Patent without exercising inventive ingenuity. In my view the Skilled Person would not.

[399] Apotex's only witness who gave evidence on double patenting was Dr. Bastin. Pfizer observes that while Apotex argues that all solid state forms of all salts were monopolized by the CA 540 Patent, Dr. Bastin did not give that evidence. Rather, Dr. Bastin testified that nothing in the prior art tells one how to prepare Form I ODV succinate specifically.

[400] Dr. Bastin gave the following evidence in cross-examination at pages 157 and 158:

> Q. Right, but nothing in the prior art tells you how to prepare Form I ODV succinate specifically?
>
> A. Not specifically, yeah.

[401] Insofar as his affidavit is concerned, while Dr. Bastin deposed to his opinion "that claim 21 of the 540 Patent includes within its scope the compound ODV succinate", his evidence relating to CA 540 and its Claim 21 does not refer to Form I ODV succinate which I have found to be the inventive concept covered by Claims 8 and 9. Dr. Bastin's testimony, nothing in the prior art, which includes CA 540, tells one how to prepare Form I ODV succinate specifically. In my view this supports the proposition that Claims 8 and 9 exhibit novelty or ingenuity.

[402] In this connection, I accept that a Skilled Person could not know from Claim 21 what the properties of any particular salt form of ODV might be. He or she would not know whether (or how) it could be made as a crystalline solid, what crystalline solids may exist, or whether any particular salt or solid form would have properties amenable to formulation and development (including a sustained release formulation). Nothing in Claim 21 pointed to specifically to Form I ODV succinate, nor indeed even to ODV succinate as a salt. The only salt form of ODV specifically taught by the 540 Patent is the fumarate, and no properties (beyond a melting point) of that salt are provided. The CA 540 Patent discloses the possibility that other pharmaceutically acceptable salts of the "compounds of the invention" could exist, but there is no specific indication that the succinate salt of ODV could be formed, would be crystalline or would have any of the properties disclosed in the 668 Patent.

[403] On further review of the evidence in this case including the invention story and knowledge of the Skilled Person as I have found them in my discussion of obviousness, I am persuaded that the Skilled Person reading Claim 21of the CA 540 Patent (together with his or her

common general knowledge) would not arrive at Claims 8 and or 9 of the 668 Patent, *i.e.*, Form I ODV succinate, without exercising inventive ingenuity. Put another way, per *Pharmascience* at para 68, Claims 8 and 9 are patentably distinct from the Claim 21 in CA 540, because it may not be said of Claims 8 and 9 that they involve no novelty or ingenuity.

[404] For the record, I note that both Pfizer and Apotex agree that the 668 Patent is not a selection patent.

[405] Therefore I am satisfied on a balance of probabilities that Apotex's allegation of double patenting is not justified.

IX. Conclusions

[406] I have found on a balance of probabilities that Apotex's allegations of invalidity due to obviousness, inutility, anticipation, overpromising and double patenting together with Apotex's allegation of non-infringement are not justified. Therefore Pfizer will have its requested Order of prohibition.

X. Costs

[407] Costs follow the cause therefore costs are payable by Apotex to Pfizer. The parties have agreed on directions regarding costs, which agreement I find reasonable, such that directions

shall issue as set out in Schedule A - Agreed Terms of Costs Order attached to these Reasons and Judgment.

XI. Confidential Reasons

[408] 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 Apotex Inc. to Pfizer Canada Inc. previously Wheth LLC, dated January 21, 2016, until the expiry of Canadian Patent No. 2,436,668.

3. Apotex Inc. shall pay Pfizer its costs of this application in accordance with Schedule A - Agreed Terms of Costs Order attached hereto.

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.

"Henry S. Brown"
Judge

Schedule A - Agreed Terms of Costs Order

Pfizer is awarded its costs of this Application 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  Cour fédérale

FEDERAL COURT

SOLICITORS OF RECORD

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