Federal Court Cour fédérale

Date: 20240207

Docket: T-151-22

Citation: 2024 FC 106

Toronto, Ontario, February 7, 2024

PRESENT: The Honourable Madam Justice Furlanetto

BETWEEN:

TAKEDA CANADA INC.

Plaintiff

and

APOTEX INC.

Defendant

and

TAKEDA PHARMACEUTICAL COMPANY LIMITED AND TAKEDA PHARMACEUTICAL USA, INC.

Defendants/Patent Holders

PUBLIC JUDGMENT AND REASONS

(Confidential Judgment and Reasons issued January 23, 2024)

I. Overview

[1] This judgment arises from a patent infringement action brought under subsection 6(1) of the *Patented Medicines (Notice of Compliance Regulations)*, SOR/93-122 [*PMNOC Regulation*s]. The patent at issue is Canadian Patent No. 2,570,916 [916 Patent]. The innovative drug relating to the action is DEXILANT®, which is used to treat heartburn associated with gastroesophageal reflux disease [GERD], as well as to heal damage to the esophagus from stomach acid.

[2] Takeda Canada Inc. [Takeda] is the "first person" in accordance with the *PMNOC Regulations*. Takeda Pharmaceuticals USA, Inc. is the registered owner of the 916 Patent and is a party to the action pursuant to subsection 6(2) of the *PMNOC Regulations*. Takeda claims that the making, constructing, using or selling by the Defendant, Apotex, Inc. [Apotex], of its dexlansoprazole oral dose capsules in strengths of 30 mg and 60 mg [Apotex Product] in accordance with Apotex's Abbreviated New Drug Submission [ANDS] Control Number 256485 will infringe at least one of claims 1, 5-8, 10-11 and 16 [Asserted Claims] of the 916 Patent. Apotex denies infringement and asserts in defence that the Asserted Claims are invalid for anticipation, obviousness, inutility, insufficiency, overbreadth, ambiguity and/or as unpatentable subject-matter.

[3] For the reasons that follow, I find that the action should be dismissed as the Asserted Claims of the 916 Patent are not infringed and are also invalid for failure to meet the disclosure requirements under subsection 27(3) of the *Patent Act* and to provide proper disclosure of the factual basis and line of reasoning to support a sound prediction of utility.

II. Background

[4] The 916 Patent is listed on the Patent Register in association with the medicine dexlansoprazole, which is the *R*-enantiomer of lansoprazole.

[5] Dexlansoprazole is one of a group of compounds known as proton pump inhibitors [PPIs] that function by inhibiting the gastric hydrogen potassium pump, known as the H^+/K^+ ATPase [proton pump] found in cells in the lining of the stomach. Activation of the proton pump results in the formation of gastric acid which decreases the pH in the stomach. PPIs react with acid to form a compound that inhibits the proton pump through covalent bonding. The result is a decrease in the gastric acid level and a corresponding increase in the pH in the stomach.

[6] Dexlansoprazole is the active ingredient in Takeda's product DEXILANT®. DEXILANT® is a pulsatile release formulation sold in capsule form that includes two types of delayed-release beads containing dexlansoprazole. The dexlansoprazole is released from the dosage form in two discrete pulses, with one of the types of delayed release beads designed to release drug after it reaches the proximal small intestine and the second type of delayed release bead designed to release drug in the distal region of the small intestine, several hours later.

[7] Takeda obtained a Notice of Compliance [NOC] and began selling DEXILANT® in Canada in 2010. At the time DEXILANT® entered the Canadian marketplace it was the sixth PPI available, with the market already including other PPIs, namely omeprazole, esomeprazole, lansoprazole, pantoprazole (and pantoprazole magnesium) and rabeprazole, which were sold as

single release formulations for treating GI disorders related to increased and delocalized gastric acid.

[8] This action initially alleged infringement of two patents listed on the Patent Register – the 916 Patent and Canadian Patent No. 2,671,369 [369 Patent]. However, by letter dated June 12, 2023, Takeda advised the Court that it would not be pursuing the allegations in respect of the 369 Patent. At trial, Takeda confirmed that it had abandoned its infringement claim with respect to the 369 Patent and that there were no issues for the Court to determine with respect to the 369 Patent.

III. The 916 Patent

[9] The 916 Patent is entitled "Pulsed Release Dosage Form of a PPI". It is the national phase entry of a Patent Co-operation Treaty patent application filed on June 1, 2005, which is based on a United States priority patent application, filed on June 16, 2004. The application for the 916 Patent was published on January 26, 2006 and will expire on June 1, 2025. It names two inventors: Dr. Majid Vakilynejad (a pharmacokineticist) and Dr. Rajneesh Taneja (a formulator).

[10] Page 1 of the 916 Patent identifies the technical field of the invention of the 916 Patent as relating to PPIs and in particular, dosage forms containing multiple doses of a PPI.

[11] The Background to the 916 Patent describes PPIs as a class of pharmaceutical compounds that inhibit gastric acid secretion by inhibiting the proton pump. It notes that PPIs rapidly degrade in acidic environments and therefore that dosage forms containing PPIs are

generally designed to protect the PPI from the acidic environment of the stomach and to release the PPI in the upper small intestine.

[12] The Background explains that PPIs have a prolonged therapeutic effect that does not directly correlate with serum concentrations of these drugs and their relatively short pharmacokinetic [PK] half-life. It further explains that despite the prolonged therapeutic effect of PPIs, some patients on PPI therapy experience a nocturnal breakthrough event where the secretory activity of the proton pump returns. The Background states that there is no currently known solution to nocturnal breakthrough effects and that there is a need for a dosage form containing a PPI that can provide a full day of therapeutic effect while being administered on a once-a-day basis.

[13] The Summary of the Invention [Summary] describes the invention of the 916 Patent as dosage forms comprising a PPI that is released as a first and a second dose in an amount sufficient to raise the plasma concentration of the PPI to at least 100 ng/mL. The Summary explains that release of the PPI may occur as discrete pulses where the pulses are separated by a pre-selected period of time or alternatively, may be separated by little or no time delay and released continuously. The Summary states that the invention also provides “methods of treating gastrointestinal disorders with the dosage forms”.

[14] In the Detailed Description [Description], the 916 Patent teaches the person skilled in the art [PSA] that the PK properties of the PPI can be used to mitigate the nocturnal breakthrough phenomenon so that a single oral dosage form can be taken once a day. First, it teaches that

alleviation of nocturnal breakthrough is a function of the concentration of the PPI in the patient; and second, it teaches that there is a threshold concentration that must be surpassed in a second dose of the PPI before a therapeutic effect is achieved (916 Patent, Ex1, 2a:8-17):

> It has unexpectedly and surprisingly been discovered that the breakthrough phenomenon can be mitigated through appropriate use of pharmacokinetic properties of these drugs to establish effective concentrations of the PPI. In particular, it has been found that it is not sufficient merely to provide an additional dose of PPI sometime after a first daily dose and before nighttime. The appropriate means for alleviating the breakthrough phenomenon is a function of the concentration of the PPI in a patient. Applicants have discovered that there is a threshold concentration of these drugs that must be surpassed in a second dose of the PPI before a therapeutic effect is achieved. Moreover, the first and the second dose can be administered in a single oral dosage format that can be taken once a day to alleviate nocturnal breakthrough events.

[15] The invention is described as providing a dosage form where each of the first and second dose of PPI is "in an amount sufficient to achieve a therapeutic effect and thereby alleviate the nocturnal breakthrough phenomenon" (916 Patent, Ex1, 2a:18-21). The Description teaches that each dose of PPI should raise the plasma level of PPI to at least 100 ng/mL, preferably above 200 ng/mL, more preferably above 300 ng/mL, even more preferably above 400 ng/mL, and most preferably above 500 ng/mL (916 Patent, Ex1, 3:1-5). The 916 Patent notes that "those skilled in the art can readily determine the milligram amounts of any particular PPI that should be included in the first and second dose of the PPI to raise patient plasma levels to the thresholds" (916 Patent, Ex1, 3:5-7).

[16] The PSA is told that the benefits of the invention are not limited to a particular type of dosage form and that the dosage forms of the invention can exist as either controlled release dosage forms or pulsed release systems. Controlled release dosage forms are described as

including matrix systems, osmotic pumps and membrane controlled systems. Pulsed release systems are described as generally comprising a first drug release and second drug release separated by a predetermined period of time or site of release. The 916 Patent notes that this may include a combination of an immediate release and extended release formulation and can include particle or granule systems where distinct populations of drug containing particles are used to achieve the pulsed release with different coating polymers targeted to release the drug at different points in time or location (916 Patent, Ex1, 10:23-11:3).

[17] The 916 Patent teaches that when a pulsed release dosage form is employed, the first and second pulses of the drug should each be sufficient to increase the plasma level concentration above the threshold level (916 Patent, Ex1, 12:4-6). The 916 Patent explains that due to decreasing absorption in the downstream portions of the gastrointestinal [GI] tract, it is preferred to load dosage forms with PPI such that the second dose of PPI is higher than the first dose (916 Patent, Ex1, 12:25-27). The 916 Patent teaches a second dose that is at least 10% more, more preferably at least 50% more, even more preferably at least 100% to 200% more, and most preferably at least 200% to 900% more than the first dose (916 Patent, Ex1, 12:27-31). The 916 Patent states that a PSA would be able to formulate oral dosage forms containing a PPI that is released in accordance with the threshold concentrations (916 Patent, Ex1, 11:28-30).

[18] The 916 Patent teaches that any PPI can be used in the dosage form as well as their respective enantiomers (916 Patent, Ex1, 2a:22-27). It refers to lansoprazole or an enantiomer or salt thereof such as *R*-lansoprazole (dexlansoprazole) as a PPI of the invention (916 Patent, Ex1,

2:24-25). The 916 Patent states that the dosage forms may be tested empirically in animal and/or human models (916 Patent, Ex1, 13:27-28).

[19] The 916 Patent includes two examples. The first example refers to mathematical modelling based on plasma concentration data from administration of single intravenous [IV] doses of lansoprazole in humans. The example refers to using the IV data to model the pharmacological effect "using a sigmoid E_{max} model", and modelling PK using a two compartment model with a PK compartment linked to a separate effect compartment. The example refers to the modelling first establishing "the pharmacokinetic characteristics of lansoprazole", then "the relationship between drug plasma concentration and intragastric pH", and then "pharacodynamic [sic] parameter estimates" (916 Patent, Ex1, 14:24-26). The results of the modelling are depicted graphically in Figure 1 of the patent, which is described as showing the relationship between plasma concentration at steady-state and gastric pH and as establishing that the threshold concentration of "approximately 100 ng/mL should be attained for purposes of attaining a minimum change in the desired pharmacological effect from baseline." (916 Patent, Ex1, 14:32-15:2).

[20] The second example is a site of absorption study that measures the extent to which lansoprazole was absorbed at different sites in the GI tract (916 Patent, Ex1, 15:5). The 916 Patent states that Example 2 shows that "[t]he rate and extent of absorption for lansoprazole from the distal small intestine [is] less than that obtained for the proximal intestine" and that "[t]he extent of absorption was reduced when lansoprazole was directly delivered to the colon." (916 Patent, Ex1, 17:1-3).

IV. Issues

[21] The following issues were identified by the parties as being those in dispute for this action:

A. The construction of the Asserted Claims, and specifically, the meaning to be given to the elements: “a first and a second dose” and “threshold concentration”;

B. Whether the making, constructing, using or selling of the Apotex Product in accordance with ANDS Control Number 256485 would infringe the Asserted Claims?

C. Whether Canadian Application No. 2,499,574 [574 Application] anticipates the subject-matter defined by the Asserted Claims, contrary to paragraph 28.2(1)(b) of the *Patent Act*?

D. Whether the subject-matter defined by the Asserted Claims would have been obvious on the claim date of June 16, 2004 to a PSA, contrary to section 28.3 of the *Patent Act*?

E. Whether a practical utility relating to the subject-matter of the Asserted Claims was not soundly predicted by the 916 Patent’s Canadian filing date of June 1, 2005?

F. Whether the 916 Patent fails to correctly and fully describe the invention and its operation or use as contemplated by the inventors, contrary to subsection of 27(3) of the *Patent Act*?

G. Whether the Asserted Claims are broader than either the invention made by the named inventors of the 916 Patent or the invention disclosed in the specification of the 916 Patent?

H. Whether the Asserted Claims fail to define distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed, contrary to subsection 27(4) of the *Patent Act*? and

I. Whether the Asserted Claims claim patentable subject-matter, as required by section 2 of the *Patent Act*?

V. Witnesses

[22] Five experts gave testimony at the trial of this action; two experts gave evidence for Takeda (Dr. Robert J. Timko and Dr. David Armstrong) and three experts for Apotex (Dr. Colin Rowlings, Dr. Neal Davies and Dr. Peter Kahrilas).

[23] As a preliminary matter, I note that Apotex challenged the admissibility of much of Takeda's expert evidence. While I have determined that the expert evidence should not be rendered inadmissible, I have concerns with certain aspects of Takeda's expert evidence and attribute those aspects limited weight as set out further below. A summary of these findings follows.

A. *Takeda's Experts*

[24] **Dr. Robert J. Timko –** Dr. Timko obtained his Ph.D. from Rutgers University in 1979, specializing in dissolution, formulation development, and physical pharmacy. He is currently the Founder and President of RhoTau Pharma Services LLC, a pharmaceutical and regulatory sciences consulting firm. Dr. Timko has over 45 years experience working in pharmaceutical formulation and process development for new chemical entities, generics, and consumer (over-the-counter) products, including 30 years with AstraZeneca. He was admitted as an expert in pharmaceutical formulation, with expertise in respect of the design, development, manufacture and analysis of pharmaceutical dosage forms.

[25] Dr. Timko delivered three expert reports in the proceeding. His first report opined on claims construction and infringement. The second report opined on the validity of the 916 Patent, including the issues of sufficiency and overbreadth and responded to the expert report of Dr. Rowlings on those issues. The second report also commented on documents relating to DEXILANT® and whether DEXILANT® was covered by the claims of the 916 Patent. The third report replied to certain comments made by Dr. Rowlings and Dr. Davies on infringement.

[26] Dr. Timko was unable to comment on the full scope of Dr. Rowlings' and Dr. Davies' critiques of his infringement analysis. During cross-examination, he acknowledged that he did not read the whole of their reports, but only those aspects to which he responded. His evidence therefore did not benefit from a full understanding of the completeness of Dr. Rowlings' and Dr. Davies' comments.

[27] In final argument, Apotex challenged the admissibility of Dr. Timko's infringement opinion, asserting that he had employed a novel untested methodology. In his infringement analysis, Dr. Timko identified certain individual plasma concentration curves amongst the bioequivalence test data on the Apotex Product that, in his view, showed that the dexlansoprazole within the Apotex Product was released as two distinct pulses. To determine the amount of dexlansoprazole present in each of the asserted doses (or pulses), Dr. Timko identified a proposed transition point between the two asserted releases and then estimated the "area under the curve" [AUC] for each proposed pulse using the trapezoidal mathematical integration method. The amount of dexlansoprazole in each proposed dose was then determined from the estimated AUC exposure values using the total, starting dose amount.

[28] Apotex asserts that Dr. Timko's analytical approach is a novel testing methodology that does not meet the reliable foundation test laid down by the U.S. Supreme Court in *Daubert v Merrell Dow Pharmaceuticals, Inc*, 509 US 579 (1993) [*Daubert*] and cited with approval by the Supreme Court of Canada [SCC] in *R v J-LJ*, 2000 SCC 51 [*J-LJ*] at paras 33-35. In *J-LJ*, the SCC identified four factors that must be considered when evaluating whether a novel test methodology will be accepted by the Court as admissible evidence: 1) whether the theory or technique can be and has been tested; 2) whether the theory or technique has been subjected to peer review and publication; 3) the known or potential rate of error or the existence of standards; and 4) whether the theory or technique used has been generally accepted.

[29] While I accept many of the concerns raised by Dr. Davies and Dr. Rowlings as to the approach taken by Dr. Timko in his analysis, and while I find that the cross-examination further

undermined Dr. Timko's approach, in my view these issues are best addressed as a matter of weight, rather than admissibility.

[30] First, I do not accept that Dr. Timko has introduced a new methodology as that term was intended in *Daubert*. His analysis does not involve the development of a new protocol or experimental procedure, but rather involves an attempt to adapt known analytical techniques (*i.e.*, AUC and trapezoidal method) to a new context – that of determining whether the dose amounts claimed are found in the Apotex Product. Indeed, Apotex' expert Dr. Davies referred to AUC in his scientific primer as a known PK parameter, reflecting "the total exposure of the body to the drug" and discussed the trapezoidal method for determining AUC (Davies, Ex32, para 91). As discussed further below, while the approach taken by Dr. Timko was shown to have flaws, Apotex' criticisms do not, in my view, engage the *Daubert* principles.

[31] Second, while Apotex argues that Dr. Timko's analysis taints the whole of his infringement opinion such that his full report should be rendered inadmissible, I do not accept that it extends this far. The determination of the dose amounts of dexlansoprazole is but one part of Dr. Timko's infringement assessment. It is clear that Dr. Timko is an expert in his field and that he has provided some useful information for the Court's consideration. I do not accept that the whole of his report is subject to concern for admissibility.

[32] Third, I consider Apotex' argument to arise too late in the day to be dealt with as an admissibility objection. In my view, this type of admissibility argument should have been raised with the Court as soon as Dr. Timko's evidence was received so that the Court could have

considered the proper approach to be taken and whether a *voir dire* would benefit its gatekeeper role (Rule 52.5(1), *Federal Courts Rules*). As noted in *White Burgess Langille Inman v Abbott and Haliburton Co*, 2015 SCC 23 [*White Burgess*], one of the key objectives in the Court's gatekeeping role is to streamline the process and balance relevance, reliability and necessity as against time, prejudice and confusion (at paras 16, 24). By Apotex waiting to raise its concerns, this balancing exercise can no longer serve the same objective.

[33] **Dr. David Armstrong –** Dr. Armstrong has practiced gastroenterology in the United Kingdom [UK] and Canada since 1983. He is also a Professor of Medicine at McMaster University. He obtained his medical degree from Cambridge in 1977 and completed post-graduate work at King's College Hospital Medical School. He is certified by medical boards in Canada and the UK and is a member of many medical associations relating to gastroenterology, including the American Gastroenterological Association [AGA]. He has also served as a peer reviewer for several academic publications. Dr. Armstrong was admitted as an expert in the use of PPIs in clinical, research and hospital settings and the treatment of gastric acid disorders, including the use of PPIs from the 1990s to present, including the knowledge, trends, and biases held by physicians during this period. Dr. Armstrong was asked to respond to Dr. Kahrilas' and Dr. Davies' review of the 916 Patent and their analyses on inventiveness, and to Dr. Davies opinion on anticipation. He was also asked to provide his opinion on the issue of utility and to respond to Dr. Kahrilas and Dr. Davies on this issue. Dr. Armstrong further commented on the properties and benefits of DEXILANT®.

[34] In final argument, Apotex objected to the admissibility of Dr. Armstrong's report on the basis that he had failed to fulfill his overriding duty as an expert. As set out in *White Burgess* at paragraph 32, an expert has an overriding duty to the Court to provide their evidence impartially, independently and without bias. The expert's opinion must reflect an objective assessment of the questions at hand; it must be the product of the expert's independent judgment, uninfluenced by the party who retained the expert or the outcome of the litigation; and must not unfairly favour one party's position over another. This overriding duty is reflected in the Expert Code of Conduct, which is discussed in Rule 52.2, and attached as a Schedule to the *Federal Courts Rules*.

[35] Apotex points to candid admissions by Dr. Armstrong that he did not read prior art on which his comments relating to obviousness and anticipation were based, instead relying on the summaries provided by Takeda's counsel. On cross-examination, Dr. Armstrong acknowledged that in view of this reliance he had made inaccurate statements in his report as to the content of prior art, and in particular with respect to the examples of the 574 Application and the disclosure in prior art documents, WO 03061584 A2 [WO 584] and WO 0124777 A1 [WO 777]. He admitted to relying upon information from counsel in an "unconfirmed", "unsubstantiated" and "unverified" manner and that he was not surprised by certain inaccuracies in his opinion that were brought to his attention during cross-examination. With respect to the 574 Application, Dr. Armstrong admitted that if he had taken greater care to understand this reference that he would have written certain aspects of his opinion differently. He acknowledged that he should have read the entirety of the prior art documents to provide his opinions.

[36] I agree that Dr. Armstrong's evidence on the prior art is tainted by the select reading taken, which reflects Takeda's interpretation of the references, thereby putting the impartiality and independence of his related opinions in question. The issue before the Court is whether Dr. Armstrong's evidence should be rendered inadmissible in view of these concerns or whether it should be dealt with as a matter of weight.

[37] In *Biogen Canada Inc v Taro Pharmaceuticals Inc*, 2020 FC 621; aff'd on appeal 2022 FCA 143, Justice Manson considered the issue of impartiality in the context of a patent infringement action. In that case, cross-examination revealed that approximately one hundred paragraphs of the expert's report had been copied verbatim from the Notice of Allegation, which the expert acknowledged he had never reviewed. Justice Manson found that this activity cast significant doubt as to the impartiality and independence of the expert, but dealt with these concerns as a matter of weight rather than rendering the evidence inadmissible:

> [44] As a preliminary point, the parties' key witnesses' evidence was uniformly weakened on cross-examination. Given the inconsistencies of evidence, advocacy, and unreasonable positions taken by Drs. Oh and Leist for Biogen, and Drs. Ebers and Bailey for the Defendants, unless otherwise specified, the Court gives limited weight to their expert opinion evidence.
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> [...]
>
> [70] Dr. Ebers' report was also far from impartial. Biogen highlighted approximately one hundred paragraphs of his report that were copied nearly verbatim from Taro's NOA, which Dr. Ebers acknowledged he had never reviewed.
>
> [71] It is certainly permissible for counsel to help an expert prepare his or her report (*Moore v Getahun*, 2015 ONCA 55 at paras 55, 64). Counsel may even point the expert to relevant prior art, as long as the expert reviews and confirms the content of his or her report, as the choice of prior art is entirely in the hands of the party alleging obviousness (*Ciba Specialty Chemicals Water Treatments Limited's v SNF Inc*, 2017 FCA 225 at para 60). It is

> quite another story for an expert to do little or no independent research and accept, verbatim, large portions of a NOA prepared by legal counsel which the expert has never seen, let alone reviewed. This crosses the line of propriety and puts into real doubt the impartiality and independence of the expert; key aspects of the expert's duty to the Court (*White Burgess Langille Inman v Abbott and Haliburton Co*, 2015 SCC 23 at paras 26-32).

[38] Similarly, in *Rovi Guides, Inc v Bell Canada*, 2022 FC 1388 [*Rovi*], Justice Lafrenière admitted the expert report in question despite finding that significant portions of the report were unequivocally plagiarized. Justice Lafrenière held there would be severe prejudice to Rovi in disqualifying its only technical expert, that far outweighed any prejudice to Bell in treating the criticisms of the expert's report as a matter of weight:

> [107] However, what happened in this case went well beyond collaboration, consultation, wordsmithing or editing. It was word-for-word copying of a technical expert's opinions and conclusions on key issues before this Court, all done without any attribution. It is plagiarism pure and simple. Plagiarism is wrong whether it is intentional or not.
>
> [108] A critical distinction must be drawn between counsel assisting an expert in framing their reports in a way that is comprehensible and responsive to the pertinent legal issues in a case and leading, or be seen to have led, an expert to express a particular opinion. The latter crosses the line of propriety and puts into real doubt the impartiality and independence of the expert: *White Burgess Langille Inman v Abbott and Haliburton Co*, 2015 SCC 23 [*White Burgess*] at paras 26-32. It also brings into question what other "assistance" may have been given to the expert in drafting their report. The expert's opinion "must be independent in the sense that it is the product of the expert's independent judgment, uninfluenced by who has retained him or her or the outcome of the litigation" (*White Burgess* at para 32).
>
> [...]
>
> [111] In *Abbott Laboratories v Canada (Minister of Health)*, 2006 FC 76, aff'd 2009 FCA 94 [*Abbott Laboratories*] at para 19, Associate Judge Martha Milczynski, then called Prothonotary, set out the proper approach to determine whether or

not an expert should be disqualified. In that case, the plaintiff expressed concern that a proposed expert of one of the defendants had received some confidential information of the plaintiff, thereby placing the expert in a potential conflict of interest. Prothonotary Milczynski stated that there must be an objective review of the facts and circumstances in each case and listed various factors to be analyzed in conducting the review. For the purpose of the present case, the following factors are relevant:

- whether the expert knew he or she was relying on plagiarized information;
- the nature of the plagiarized information;
- the risk of prejudice arising to either the party challenging the expert or to the party seeking to retain the challenged expert; and
- the interests of justice and public confidence in the judicial process.

[112] After balancing all of the above factors, I conclude that Mr. Wahlers should not be disqualified as a witness. The circumstances in the present case are different than those in *Anderson*. In *Anderson*, the expert report prepared by a family physician was found to be plagiarized and the physician was found to have lied about it. The judge also concluded that the expert was biased, unqualified and not independent. The primary reason the expert was disqualified was because he did not have the appropriate expertise, which is not the case here.

[113] While the second factor identified above militates in favour of disqualification, I find there would be a severe prejudice to Rovi to disqualify its only technical expert, one that far outweighs any prejudice to the Defendants.

[114] It remains that Mr. Wahlers lack of candour and his apparent indiscriminate adoption of another expert's opinions or conclusions, albeit unknowingly, raise serious concerns in my mind as to whether Mr. Wahlers has fulfilled his duty to the Court to provide an independent opinion. The problem is compounded by the fact that, contrary to what is asserted by Rovi, Mr. Wahlers was unable to defend many of his opinions at trial.

[...]

[118] Despite my strong reservations as to Mr. Wahlers' credibility, independence and impartiality, it would not be just to

> reject his reports or testimony out of hand. There are, after all, some aspects of his evidence that are not controversial and prove useful and reliable. The concerns raised by the Defendants go to weight to be given to Mr. Wahlers' evidence, rather than to its admissibility. Just to be clear, I have looked upon Mr. Wahlers' evidence with great skepticism.

[39] Applying the principles set out in *Rovi*, and considering the potential prejudice to Takeda as Dr. Armstrong was Takeda's primary expert on validity and only expert who responded to Apotex' experts Dr. Davies and Dr. Kahrilas on validity issues, I prefer to deal with his evidence as a matter of weight. While it was revealed that Dr. Armstrong did not complete a full reading of the references, it is clear that he had the requisite expertise to give evidence and that he was willing to concede the shortcomings in the approach he had taken. In my view, these concessions established that Dr. Armstrong was not functioning as an advocate for Takeda. As was the case in *Rovi*, even with these difficulties and others highlighted during cross-examination, Dr. Armstrong's views were still of value to the Court on certain technical issues. Indeed, even Apotex relied on Dr. Armstrong for specific points within its argument, acknowledging in oral submissions that they had cited to Dr. Armstrong various times.

B. *Apotex' Experts*

[40] **Dr. Colin Rowlings –** Dr. Rowlings obtained his Ph.D. from the University of Iowa in 1989, specializing in pharmaceutics. He is currently the Senior Vice President of Gossamer Bio Inc. He has over 34 years experience working in the pharmaceutical industry primarily on small-molecule, new chemical entity development, encompassing a variety of dosage forms. He has contributed to multiple product approvals and has significant experience in the field of oral modified release dosage forms, including pulse release dosage forms and the use of enteric

coatings. Dr. Rowlings was admitted as an expert in the field of pharmaceutical sciences, pre-formulation, formulation development and analytical testing, with specific expertise in oral modified release dosage forms (extended release formulations, pulsatile release formulations, gastro-retentive formulations, and mini-tablet and pellet formulations), characterization of excipients, and the design, interpretation and application of site of absorption studies. His expertise includes analysis and interpretation of PK and pharmacodynamic [PD] data from studies conducted for the purpose of developing oral formulations.

[41] Dr. Rowlings provided two reports: a first report opining on claims construction, anticipation, obviousness, overbreadth, sufficiency and ambiguity; and a second report opining on the issue of infringement and responding to Dr. Timko's evidence on this issue.

[42] Overall, I found Dr. Rowlings to be a forthright and fair witness who was knowledgeable about pharmaceutical formulation and whose testimony assisted the Court. He conceded points that were against the interests of Apotex where it was evident that he should do so. For the most part, I rely heavily on Dr. Rowlings' evidence with one reservation relating to his obviousness analysis, where he admittedly reviewed prior art references in an effort to "find" certain elements in the claims. In my view, this suggests a degree of hindsight in the approach taken to the references such that the Court must consider his evidence on this issue with some caution.

[43] **Dr. Neal Davies –** Dr. Davies is a pharmacologist and registered pharmacist with over 25 years experience in drug development, pharmacokinetics, drug delivery and pre-clinical and clinical pharmaceutical sciences. He obtained his Ph.D. from the University of Alberta in 1996,

specializing in pharmacokinetics. He is currently a Professor in the Faculty of Pharmacy and Pharmaceutical Sciences at the University of Alberta and is also a Fellow in the Canadian Academy of Health Sciences. Dr. Davies has significant experience in the analysis of plasma profiles and the use of PK models. His work focuses on drug development, pharmacokinetics and drug delivery, as well as on basic and clinical pharmaceutical sciences. Dr. Davies was admitted as an expert in the fields of pharmacology, pharmacokinetics (including drug absorption, distribution, metabolism and excretion), pharmacodynamics and pharmaceutical sciences, with specific expertise in PK/PD modelling, designing and interpreting PK/PD studies, analytical techniques to measure drug concentration, drug development, drug delivery and formulations, determining appropriate dosages in animals and humans, chirality of drugs, gastrointestinal disorders and PPIs. Like Dr. Rowlings, Dr. Davies provided two reports. His first report opined on claims construction, anticipation, obviousness, utility, overbreadth, insufficiency and ambiguity. His second report opined on the issue of infringement and responded to Dr. Timko's evidence on this issue.

[44] Dr. Davies is undoubtedly a very knowledgeable witness. He gave helpful information on pharmacology, pharmacokinetics, pharmacodynamics, including PK/PD modelling and how the PSA would read and understand Example 1 of the 916 Patent. He was the only true pharmacokinetics expert in the proceeding and the only expert who understood all facets of the effect compartment modelling that was used by the inventors. While I found Dr. Davies to be very knowledgeable, at times I found him to be unnecessarily difficult when answering straight-forward questions and to be fixated on problems which made him unable to respond meaningfully to questions directed at understanding the significance of some of his comments. I

had difficulty with his testimony regarding the calculation of the dose amounts from the 574 Application where I found he read the examples without trying to understand them in a practical way. In that instance where the evidence was in conflict with Dr. Rowlings, I preferred the evidence of Dr. Rowlings. I have highlighted these matters further in my analysis below.

[45] **Dr. Peter Kahrilas –** Dr. Kahrilas is a gastroenterologist with 40 years of clinical experience treating patients with acid-related disorders, such as GERD. He also conducts research and is a Professor of Medicine at Northwestern University where he has worked since 1999. His research concerns esophageal physiology and pathophysiology with a focus on motility disorders and GERD. Dr. Kahrilas is certified by several medical boards in the United States [US] and is a fellow of a number of medical organizations, including the AGA.
Dr. Kahrilas was admitted as an expert in the field of gastroenterology with specific expertise in the diagnosis and treatment of patients with esophageal disorders, such as GERD and esophageal motility disorders. Dr. Kahrilas provided a single expert report, offering opinions on claims construction, obviousness and utility.

[46] Dr. Kahrilas was a knowledgeable witness who provided clear and straight-forward answers, giving his responses simply and directly even if answers were not in Apotex' favour. I found Dr. Kahrilas' evidence to be helpful and where it conflicted with that of Takeda's experts, I preferred the evidence of Dr. Kahrilas unless otherwise stated below. Similar to Dr. Rowlings, the only reservation I had with Dr. Kahrilas' evidence related to his approach to the third part of the obviousness analysis and his review of prior art references in an effort to "find" elements in the claims. I discuss this concern in greater detail below.

C. *Fact Witnesses*

[47] Three fact witnesses gave evidence at trial. The first fact witness, Dr. Majid Vakilynejad, is one of the inventors of the 916 Patent. His evidence provided background on the proposed invention and Examples 1 and 2 of the 916 Patent. The remaining two fact witnesses, Jason Goodfield and Rose Guthrie, are current and former employees of Takeda who spoke to the introduction and impact of DEXILANT® on the Canadian market. Apotex objected to the admissibility of certain aspects of the Goodfield and Guthrie evidence on the basis that it was hearsay, opinion evidence, or contrary to Rule 248 of the *Federal Courts Rules*. I address these objections and provide a brief summary of the fact evidence below.

[48] In addition to Takeda's fact witnesses, Apotex introduced one fact witness affidavit from Julie Szirtes, the Director of Clinical Research and Development at Apotex. Ms. Szirtes provided an affidavit attaching several documents relating to [redacted] submitted as part of Apotex's ANDS that compared the 60 mg Apo-dexlansoprazole capsules to the 60 mg DEXILANT® capsules.

(1) Dr. Vakilynejad

[49] Dr. Vakilynejad joined Takeda Abbott Pharmaceuticals (TAP) in September 2000 and began investigating the PPI, lansoprazole, in late 2001. His role was as a member of the Drug Metabolism and Pharmacokinetics group. Dr. Taneja, the other co-inventor, worked in a separate department and was part of the formulation group. At the time, several PPIs including lansoprazole were already on the market; however, none were able to provide patients with a full day of therapeutic relief. To address nocturnal breakthrough events, Dr. Vakilynejad was asked

by Dr. Taneja to conduct mathematical modelling to determine the impact of PPIs on gastric acid pH over 24 hours.

[50] As a starting point, Dr. Vakilynejad testified that he modified a model developed at the University of Buffalo by Thomas A. Puchalski to create an exposure response analysis using the data from a Phase I oral dose study (M93-006) that looked at the effect of multiple dose regimens of lansoprazole on intragastric pH. However, this analysis failed to yield a direct relationship between intragastric pH and the concentration of lansoprazole because of various factors, including absorption and elimination rates of the drug, thus creating a counter-clockwise loop (hysteresis loop) of the data when plotted. A one compartment open model for PK, looking at lansoprazole plasma concentration versus time data, was designed to account for the absorption and elimination rates of the drug after oral ingestion.

[51] Empirical modelling was also conducted to establish systemic threshold concentrations of lansoprazole required to increase intragastric pH in the absence of food and circadian rhythm. For this, the model was first fit to data from a different clinical study (M95-306), involving IV administration of lansoprazole that included 24-hour gastric pH monitoring. As this was an IV study, absorption in the GI tract and the impact of food were not interfering factors. Again, the results initially yielded a counter-clockwise loop where no direct relationship between intragastric pH and the concentration of lansoprazole could be determined. To try to collapse the loop and unmask the relationship, Dr. Vakilynejad applied a hypothetical effect compartment with a two compartment open model.

[52] This work was followed by modelling of the oral dosing data from M93-006 to create simulations that looked at the impact of dual-pulse dosing regimens on gastric pH both for the whole day and for the nocturnal period.

[53] Dr. Vakilynejad concluded from the modelling work that intragastric pH could be increased if a dosage form provided a plasma concentration of at least 80-100 ng/mL of drug. Dr. Vakilynejad's modelling of the IV data is set out in the patent as being the basis for Example 1 and Figure 1 of the 916 Patent.

[54] In addition to the modelling work, the inventors also designed another study that measured the absorption of lansoprazole at different portions of the GI tract using gamma scintigraphy to trace the absorption of a special remote-triggered capsule containing lansoprazole and a radioactive marker. The results confirmed a slightly lower but comparable absorption of lansoprazole from the distal small intestine as compared to the proximal small intestine and reduced absorption in the colon. Results of the study were reported in Example 2 of the 916 Patent and were the basis for the inventors' determination that in a pulsatile release formulation, the second dose of PPI needed to be at least 10 percent higher than the first dose of PPI due to decreased absorption.

[55] I found Dr. Vakilynejad to be a credible witness; however, his evidence at times was brief and glossed over details relating to the modelling work conducted. This presented certain challenges as highlighted by Dr. Davies and discussed further below.

(2) Jason Goodfield and Rose Guthrie

[56] Jason Goodfield is an employee of Takeda who holds the title of "Data & Insights Lead". His affidavit attaches as Exhibit 1 a report prepared using IQVIA data (formerly referred to as IMS data) that sets out information on the number of prescriptions of DEXILANT®, and of all PPI products in Canada, from March 2011 to December 2021 [Report]. Takeda asserts that the Report and Mr. Goodfield's evidence is relevant to the issue of commercial success. While not a current employee of IQVIA, Mr. Goodfield did work at IMS Brogan (the predecessor company to IQVIA) from 2013 to 2017 and had familiarity with how data of the type attached to his affidavit was generated, although he could not speak to the generation of the specific data attached in the Report.

[57] Apotex raised two objections to the Goodfield Affidavit. First, it objected to the Report and to the paragraphs that describe how it was prepared and what it says, on the basis of hearsay (paragraphs 4, 5, 6, 9, 10 (second sentence) and 11). Second, and related to the first objection, it argued that two of the sentences from the impugned paragraphs disclosed opinion evidence.

[58] The second fact witness, Rose Guthrie, is a former employee of Takeda who was involved with the launch and marketing of DEXILANT® in Canada. Her evidence was also introduced to support Takeda's claim of commercial success.

[59] Ms. Guthrie introduced evidence relating to DEXILANT®'s launch, physician and consumer reception, and regulatory approval. As part of her affidavit, she attached a series of third party recall studies on DEXILANT® (Exhibits H through K to her affidavit), with results

prepared between October 2012 and May 2014 [Recall Studies]. Apotex objected to this evidence and to its related paragraphs, as well as to an attachment of IQVIA prescription data on the basis of hearsay and that it was opinion evidence. Three other sentences were also objected to on the basis of Rule 248 of the *Federal Courts Rules* and refusals given during discovery.

[60] It is trite law that hearsay evidence is presumptively inadmissible unless it falls under one of the recognized exceptions to the hearsay rule or meets the criteria of necessity and reliability: *R v Khelawon*, 2006 SCC 57 at paras 2, 34, and 42; *Pfizer Canada Inc v Teva Canada Limited*, 2016 FCA 161 at paras 86-87. While business records are one such exception, a party seeking to assert that a document is a business record has the onus to establish that it meets the requirements set out in subsection 30(1) of the *Canada Evidence Act*, RSC 1985, c C-5, which provides as follows:

30 (1) Where oral evidence in respect of a matter would be admissible in a legal proceeding, a record made in the usual and ordinary course of business that contains information in respect of that matter is admissible in evidence under this section in the legal proceeding on production of the record.	30 (1) Lorsqu'une preuve orale concernant une chose serait admissible dans une procédure judiciaire, une pièce établie dans le cours ordinaire des affaires et qui contient des renseignements sur cette chose est, en vertu du présent article, admissible en preuve dans la procédure judiciaire sur production de la pièce.

[61] Takeda argues that the Report and the Recall Studies are business records. While it acknowledges that the Report was prepared for the purposes of the litigation, it argues that the underlying data exists independently as a business record and was downloaded from a repository within Takeda that is maintained in the usual and ordinary course of business. It asserts that Mr.

Goodfield has extensive experience with IQVIA/IMS data and was qualified to answer Apotex' questions. It further asserts that the Court has recognized IMS data as an independent source of reliable evidence.

[62] Both parties directed the Court to the decision in *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2018 FC 259 [*Hospira FC*], in which the Court commented on the admissibility of IMS data. In that case, the Court did not find the IMS data to fall within the business record exception; however, it nonetheless found the data necessary and reliable and to be corroborated by other evidence that was before the Court. As stated in the decision:

> [305] The IMS data does not fall within the business record exception to hearsay for the reasons described in *Eli Lilly Canada Inc v Teva Canada Limited*, 2017 FC 88 at para 18, 279 ACWS (3d) 763:
>
> > In my view, the Deloitte report does not meet the test for the business records exception. That exception requires that the author of the record have a duty to create it, and did so contemporaneously and based on personal knowledge (*Ares v Venner*, [1970] SCR 608 at p 626; see also *Canada Evidence Act*, RSC 1985, c C-5, s 30). Since the author of the Deloitte report is unknown and the details surrounding the report's preparation were not in evidence, the report cannot meet these criteria.
>
> [306] However, the IMS data is information that is commonly put into evidence in patent cases in the Federal Court. I find that this evidence is necessary and reliable.
>
> [307] With respect to necessity, I observe that Kennedy did not call any witnesses with direct knowledge of combination treatment (such as patients or prescribing rheumatologists). Kennedy's witness Bensen was forced to conclude, in cross-examination, that he had no real knowledge of how many patients at his clinics were receiving combination therapy with MTX and Inflectra.

> [308] Nonetheless, I find that this IMS data evidence is necessary. A patient or a medical professional would not be able to give the overview provided by the IMS data with respect to the approximate percentage of patients on combination treatment. Bensen attempted, but was ultimately unable, to provide this type of evidence (i.e., are the majority of patients receiving Inflectra also receiving combination treatment?).
>
> [309] Further, this evidence is reliable because, as discussed in *Bradshaw*, it is corroborated by the other evidence in this case. Hospira states that about 100 patients have received Inflectra in Canada. The IMS data is therefore consistent with the party's own admission – it shows that 93 patients have received Inflectra in Canada.
>
> [310] Moreover, the entirety of the evidence put forward in this case tends to confirm the reliability of the IMS data. As noted during the trial, IMS data is a common source of evidence in these types of trials and its reliability is generally accepted by the Federal Court.
>
> ...
>
> [330] Hospira argued that a number of conclusions Kennedy wishes to draw from the IMS data are speculative. This may be true if the IMS data were considered in isolation; however, the other evidence in this case (including the product monograph and the product label) supports the interpretation that this data shows that at least some patients are receiving adjunctive therapy with Inflectra and MTX.

[63] While the admissibility of the IMS data in *Hospira FC* was challenged on appeal (reported at 2020 FCA 30 [*Hospira FCA*]), the Federal Court of Appeal [FCA] found it unnecessary to address the hearsay argument based on the additional evidence that already supported the Judge's conclusion on the use of Inflectra (at paragraphs 27-28). Thus, the admissibility finding made in *Hospira FC* was not substantively reviewed.

[64] In my view, neither the Report nor the Recall Surveys fall within the business record exception. The Report was prepared for the purpose of litigation and not out of a duty to create it.

While it relies on IQVIA data, such data was commissioned for purchase. It is not data that was generated for Takeda in the ordinary course of business. Similarly, the Recall Surveys are not records that were created by Takeda itself in the usual and ordinary course of business. Rather, Takeda hired third party companies to generate this data. The FCA recently found brand awareness surveys inadmissible as business records in *Clorox Company of Canada, Ltd v Chloretec SEC*, 2020 FCA 76 at paragraphs 26-27. In that case, the affiant's business knowledge of the existence and contents of the surveys did not alleviate concerns about their relevance and methodology. I consider the Recall Surveys to be of the same vein. Contrary to Takeda's assertion, Ms. Guthrie is not in a position to speak to these surveys as she did not conduct them.

[65] There is also, in my view, insufficient evidence to otherwise establish necessity and reliability. While Takeda argued that the IQVIA data was necessary because there was no one witness who could speak about the market, it did not put forward any evidence as to the availability of the authors of the Report or the Recall Surveys to provide evidence. Further, although the jurisprudence suggests some general acceptance of IMS/IQVIA data due to its common usage in patent cases and its nature (*Hospira FC* at para 306; see also *AstraZeneca Canada Inc v Canada (Minister of Health)*, 2004 FC 1277 at para 11), unlike in *Hospira FC*, there was no independent evidence to corroborate the alleged market share growth of DEXILANT® or otherwise support the reliability of the IQVIA data. While Mr. Goodfield, as a former employee of IMS, was able to address certain issues relating to the computation of the data, his evidence also highlighted several unknowns, particularly as it related to the nature of the prescriptions that comprised the data and the details of the market. There was similarly no evidence to otherwise corroborate the Recall Surveys.

[66] Even if the data was deemed to meet the requirements of necessity and threshold reliability, I find the evidence to be of limited probative value to establish commercial success. First, as mentioned, there are unknowns associated with the data which undermine its usefulness. Second, the numbers proposed by IQVIA suggest at most only modest market share growth and is devoid of information as to the money spent on advertising and promotion. Third, and moreover, to establish commercial success, it must be clear that success is the result of the invention itself and not because of some other advancement associated with the product: *Tearlab Corporation v I-MED Pharma Inc*, 2019 FCA 179 [*Tearlab*] at para 69. In this case, further evidence suggests that any commercial success may be attributed at least in part to there being no food effect associated with the drug such that it could be taken at any time of day, with or without food (TT 8A, 1111:2-1112:14). This effect is highlighted along with the dual release dosage form in Takeda's marketing materials and in publications, and is separately claimed in Canadian Patent No. 2,702,356 (Guthrie, Ex40, Exhibits Q and R; TT 8A, 1113:1-6, 1114:8-21; TT 1A, 60:26-63:6, 70:28-72:6; 356 Patent, Ex5). Thus, it not clear to what extent any perceived increase in market share for DEXILANT® could be attributed to the proposed invention of the 916 Patent.

[67] On the basis of these findings, it is my view that the impugned evidence should be excluded. As such, and as agreed by the parties, I need not go on to consider the opinion evidence objections.

[68] The remaining objection to the Guthrie affidavit relates to statements in her affidavit where she describes the purported benefits of DEXILANT® that were set out in Takeda's

marketing and sales documents (Exhibits L to R to the Guthrie affidavit). Rule 248 of the *Federal Courts Rules* provides that where a party examined for discovery has refused to answer a proper question, the party may not introduce the information sought by the question at trial without leave of the Court. Apotex points to paragraphs from Takeda's Reply where Takeda alleges commercial success and refers to the success being attributable to "the properties and advantages of the subject-matter of the Asserted Claims" and to DEXILANT® providing patients with "a significantly beneficial treatment option". Questions relating to the meaning of these statements were refused on discovery on the basis that they sought opinion evidence. In my view, the impugned sentences from the Guthrie affidavit go directly to the refused information (the alleged benefit of the Apotex Product) and invoke Rule 248. Such statements cannot be introduced into evidence in view of the objections taken. I therefore agree that the first sentence of paragraph 22 and the third and fourth sentences of paragraph 23 should be excluded from the Guthrie affidavit.

VI. Claims Construction

[69] The first task for the Court in a patent infringement action is to construe the claims in issue. Claims construction is not a results-oriented exercise. Rather, the claims are to receive one and the same interpretation for all purposes: *Whirlpool Corp v Camco Inc*, 2000 SCC 67 [*Whirlpool*] at para 49(b).

[70] The focus of claims construction is on the language of the claims: *Free World Trust v Électro Santé Inc*, 2000 SCC 66 [*Free World Trust*] at para 39. The specification describes the invention so that a PSA can understand what the invention is and, when the patent expires, put it

into practice, but it is the claims that carve out the boundaries of the proprietary right granted by the patent: *Free World Trust* at para 33; *Merck & Co, Inc v Pharmascience Inc*, 2010 FC 510 at para 44.

[71] Purposive construction involves the Court trying to understand the inventor's objective intention and the particular words or phrases in the claims that describe what the inventor considered to be the essential elements of the invention: *Whirlpool* at para 45; *Free World Trust* at para 31(e); *Biogen Canada Inc v Pharmascience Inc*, 2022 FCA 143 [*Biogen*] para 74. The interpretative task of the Court is two-fold: to separate and distinguish between the essential and non-essential elements so that legal protection is given only to the essential elements of the invention claimed (*Free World Trust* at paras 15 and 31(e); *Tearlab* at para 31); and, to ascertain what is meant and encompassed by the essential elements so that the invention as claimed is properly characterized: *Biogen* at para 74.

[72] To ascertain the inventor's objective intention, however, purposive construction involves looking at the words of the claims in context, which includes the claims individually and as a whole, and considering their purpose, as well as, the patent's description: *Biogen* at paras 71-72; *Whirlpool* at para 49(e). Although the entire patent must be considered, the disclosure should not be used "to enlarge or contract the scope of the claims as written and … understood": *Whirlpool* at para 52; *Free World Trust* at para 32. Adherence to the claim language allows the claims to be read in a way in which the inventor is presumed to have intended, thereby promoting fairness and predictability: *Biogen* at para 72; *Free World Trust* at paras 31(a), (b) and 41.

[73] The objective of the analysis is to interpret and respect the inventor's objective intention as manifested in the words of the claims used, being neither benevolent nor harsh, but rather seeking a construction that is reasonable and fair to both the patentee and the public: *Biogen* at para 73; *Consolboard Inc v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504 at p 520; *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60 [*Teva*] at para 50; *Tearlab* at para 33. The words of the claims are to be read in an informed way, with a mind willing to understand, and in a way that is sympathetic to accomplishment of the inventor's purpose, expressed or implicit in the text of the claims: *Free World Trust* at paras 31(c) and 44. However, as highlighted in *Free World Trust* at paragraph 51, "...if the inventor has misspoken or otherwise created an unnecessary or troublesome limitation in the claims, it is a self-inflicted wound. The public is entitled to rely on the words used *provided* the words used are interpreted fairly and knowledgeably." [Emphasis in the original.]

[74] Although the claim language must be read through the eyes of a PSA, as equipped with their common general knowledge [CGK] (*Free World Trust* at paras 44-45; *Tearlab* at para 32), a Court is entitled to differ from the construction put forward by either party in arriving at its construction as it is the task of the Court alone to construe the claims as a matter of law: *Biogen* at para 73; *Whirlpool* at para 61. The role of experts are to put the judge in the best position to do so in an informed and knowledgeable way: *Biogen* at para 73; *Whirlpool* at para 57.

[75] I will now go on to consider the PSA and the nature of their CGK before engaging in the claims construction exercise.

A. *PSA of the 916 Patent*

[76] The PSA is a hypothetical person to whom the patent is addressed. This may be a single individual or a team of individuals representing different disciplines, depending on the nature of the invention: *Pfizer Canada Inc v Pharmascience Inc*, 2013 FC 120 at para 28. The PSA is deemed to be 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, aff'd 2015 FCA 158, rev'd on other grounds 2017 SCC 36. It is the person, or team of individuals, that would work the patent in a real sense: *Alcon Canada Inc v Cobalt Pharmaceuticals Company*, 2014 FC 462 at para 37.

[77] By the time of final argument both parties agreed that the PSA comprised a team of individuals having knowledge in: drug product formulation, with experience making different types of dosage forms using different formulation technologies; pharmacokinetics, with experience in mathematical modelling; and PPI treatment as either a medical doctor or gastroenterologist.

[78] Each party provided evidence from a pharmaceutical formulator (Dr. Timko (Takeda) and Dr. Rowlings (Apotex)) and a gastroenterologist (Dr. Armstrong (Takeda) and Dr. Kahrilas (Apotex)). However, as noted earlier, it was only Apotex who provided expert evidence from a pharmacokineticist or PK specialist (Dr. Davies).

[79] Takeda submitted that expert evidence from a PK specialist was not necessary as Dr. Vakilynejad, the inventor, was a PK specialist and had provided all of the necessary evidence from this perspective. While Dr. Vakilynejad was equipped to provide factual background as to the development of the invention, it is the skilled person who must interpret the patent, including its examples. The inventor by nature is not independent and cannot step into the shoes of the PSA to provide a neutral interpretation of the patent's teachings: *Merck Frosst Canada Inc v Canada (Minister of National Health and Welfare)*, [1998] FCJ No 1882, 160 FTR 161 (FC) at para 22. As discussed further below, the absence of expert evidence from Takeda in this area leaves a void in aspects of their analysis.

B. *CGK of the PSA*

[80] To properly equip myself for the claims construction exercise, I must consider the CGK of the PSA. CGK is the knowledge generally known at the relevant date by the PSA to whom the patent relates. However, it does not include all information in the public domain: *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 [*Sanofi*] at para 37; *Bell Helicopter Textron Canada Limitée v Eurocopter, société par actions simplifiée*, 2013 FCA 219 [*Bell Helicopter*] at paras 64-65.

[81] CGK is relevant to both the purposive construction of the claims, as well as to my analysis on obviousness, which will come later. It has been described as the information that a PSA would become aware of and accept as a "good basis for further action": *Mylan Pharmaceuticals ULC v Eli Lilly Canada Inc*, 2016 FCA 119 [*Mylan*] at para 24. As no expert suggested a substantial change in CGK between the relevant date for obviousness (June 16,

2004) and that for construction (the publication date of January 26, 2006), I will address the CGK as of this earlier date.

[82] In general, there was little dispute as to what comprised the CGK, which can be summarized as follows.

[83] The PSA knew about PPIs and their mechanism of action as set out in the background section above, and was aware of their usefulness to treat GI disorders, such as esophageal disease, GERD, peptic and gastric ulcers and reflux disease. It was known that non-human mammals suffered from the same types of GI disorders as humans and that PPIs could be effective in both humans and animals for treating GI disorders. By 2004, known PPIs included omeprazole, esomeprazole, lansoprazole, pantoprazole and rabeprazole, all of which were on the market as single release dosage forms that released drug after it passed through the stomach into the proximal intestine. While dexlansoprazole was known to be a PPI and the *R*-enantiomer of lansoprazole, it was not yet on the market as part of an approved medicine.

[84] The gastroenterologist who was part of the skilled team was also aware of different dosing strategies that had been used to address nocturnal breakthrough events, including multi-day dosing. Such multi-day dosing could involve administering the same dose that had been administered a second time, or splitting the dose by administering the same total dosage amount over the course of the day, but giving half in the morning and half in the evening.

[85] As PPIs were known to be unstable in acid, the PSA knew that dosage forms containing PPIs had to be protected from the acidic environment of the stomach through the use of an enteric coating that dissolved at pH values higher than those in the stomach. The PSA was aware of a number of approaches for formulating delayed release dosage forms, including those that released PPIs. It was known that pulsatile release formulations delivered two doses from one dosage form and could be made for PPIs; however, none were yet on the market.

[86] The PSA knew how to design a PK model to evaluate PK properties – *i.e.*, absorption, distribution, metabolism and elimination; and how to measure PK parameters, such as bioavailability, AUC, C_{max} (the maximum concentration of drug in the bloodstream after it has been administered) and T_{max} (the time taken for a drug to reach its C_{max}). By 2004, the PSA knew that while each PPI had a different C_{max} value after being administered, the drug's therapeutic effect lasted longer than their pharmacokinetic half-life.

[87] The PSA knew about the study of pharmacodynamics and how drugs affect physiological processes in the body such as gastric acid function. The PSA knew about PK/PD mathematical modelling and how it was used to understand the relationship between drug concentration in the body and pharmacological effect, as well as to predict optimal dosing. One compartment and two compartment models had been used along with effect compartment modelling for the purpose of collapsing a hysteresis loop.

[88] The PSA also knew that the small intestine was the principal site of absorption for drugs and that it included three regions (duodenum, jejunum and ileum) that gradually increased in pH

from around 4 to 8. The stomach was known to have a much more acidic pH which could be dramatically altered by the presence of food. It was recognized that the transit time of a drug through the small intestine was 3-4 hours in both fasted and fed states, while the transit time through the stomach could vary between 0.5 and 12 hours and could be slowed by food and affected by the size of the dosage form; although, the absorption of PPIs in the small intestine had not yet been studied.

[89] As of June 2004, the PSA's CGK, thus, included knowledge of:

- PPIs and how they function in the body to treat GI disorders;
- Pulsed release dosage forms and how to make them;
- PK and PD properties and how to measure such properties using effect compartment modelling; and
- Transit times and the pH environment in the small intestine.

C. *Construction of the Asserted Claims of the 916 Patent*

[90] Armed with the CGK of the PSA, I will now go on to construe the claims. The Asserted Claims of the 916 Patent include claims 1, 5-8, 10-11 and 16, which read as follows:

> 1. A dosage form comprising a PPI wherein the PPI is released from the dosage form as a first and a second dose, wherein the first and second dose are released from the dosage form as discrete pulses of the PPI, wherein each pulse of the PPI is sufficient to raise plasma concentrations above a threshold concentration of at least 100 ng/mL, wherein the second dose contains at least 10% more of the PPI than the first dose, and wherein the first and the second dose independently comprise between 5 mg and 300 mg of the PPI.
>
> 5. The dosage form of any one of claims 1 to 4 wherein each pulse of the PPI is sufficient to maintain plasma

concentrations above the threshold concentration of at least 100 ng/mL for at least 30 minutes.

6. The dosage form of any one of claims 1 to 5 wherein the second dose contains at least 50% more than the first dose.

7. The dosage form of any one of claims 1 to 5 wherein the second dose contains at least 100% to 200% more than the first dose.

8. The dosage form of any one of claims 1 to 5 wherein the second dose contains at least 200% to 900% more than the first dose.

10. The dosage form of claim 1 wherein each of the first and second dose comprise a sufficient amount of the PPI to raise plasma levels of the PPI to a threshold concentration of at least 200 ng/mL.

11. The dosage form of claim 1 wherein each of the first and second dose comprise a sufficient amount of the PPI to raise plasma levels of the PPI to a threshold concentration of at least 450 ng/mL.

16. The dosage form of claim 15 wherein the PPI is the *R*-enantiomer of lansoprazole.

[91] Claim 1 is the only independent claim and claim 16 is the claim that is specifically directed to dexlansoprazole.

[92] The parties assert, and I agree, that all elements of the Asserted Claims are essential, with claim 1 reciting the following required elements:

1. A dosage form that includes a PPI

2. the PPI is released as a first and a second dose

3. the first and second dose are released as discrete pulses

4. each pulse of the PPI is sufficient to raise plasma concentrations above a threshold concentration of at least 100 ng/mL

5. the second dose contains at least 10% more of the PPI than the first dose; and

6. the first and the second dose independently comprise between 5 mg and 300 mg of the PPI

[93] There is general agreement as to the PSA's understanding of these essential elements, including that the first and second doses being released from the dosage form as two *discrete* pulses means that the doses appear as two distinguishable peaks on a plasma concentration-time profile.

[94] However, there is disagreement relating to the interpretation to be given to two terms originating in claim 1: a) the meaning of "a first and a second dose"; and b) what is meant by "a threshold concentration" and whether, as used in the claims, it is restricted to humans.

[95] The parties assert and I agree that claims 5-8, 10-11 and 16, as they depend from claim 1, add the recited additional limitations, which are all essential elements of those claims. To the extent there are claim terms used in claims 5-8, 10-11 and 16 that are the same as terms used in claim 1, they have the same meaning: *Nova Chemicals Corporation v Dow Chemical Company*, 2016 FCA 216 [*Nova Chemicals*] at para 82.

[96] The following discussion will address the claim elements in dispute.

(a) *"a first and a second dose"*

[97] Apotex asserts that "a first and a second dose" relate to distinct amounts of PPI that are loaded into the dosage form prior to administration and that are available to be released from the dosage form upon administration. Takeda asserts that "a first and a second dose" refers to the

amounts of PPI released from the dosage form after administration devoid of its loading. In my view, both the expert evidence and the 916 Patent favour Apotex' position.

[98] As highlighted by Dr. Rowlings, "[t]hat each "dose" corresponds to a distinct dose amount within the dosage form itself ... is ... consistent with how the skilled formulator would understand the 916 Patent. For example, the first sentence of the 916 Patent states that its invention relates to "proton pump inhibitors and in particular, relates to dosage forms *containing* multiple doses of a proton pump inhibitor" (page 1, lines 4-5; *emphasis* added)." (Rowlings, Ex25, para 133).

[99] As explained by Dr. Davies, in order to have release of a first and second dose of PPI from the dosage form, the first and second dose must be contained in the dosage form (TT 6A, 707:17-18). I agree, this is a matter of logic. Consistent with this view, the 916 Patent speaks to each dose of PPI being present in the dosage form in an amount sufficient to raise the plasma levels of the PPI to at least 100 ng/mL (916 Patent, Ex1, 2:3-4; 2a:18-19). The description refers to loading the dosage form with drug for each pulse or dose (916 Patent, Ex1, 12:19-27):

> ... As further guidance, however, in cases where a pulsed release dosage form is employed, drug loading for each pulse is independently and typically between 5 mg and 300 mg, more typically between 20 mg and 200 mg. In cases where an extended release dosage form is employed, typical drug loading for the combined first and second PPI dose in such a formulation will be in the range of 50 mg to 1000 mg, and more typically 75 mg to 500 mg.
>
> It has also been discovered, that due to the decreasing absorption in the downstream portions of the gastrointestinal tract, it is preferred to load the dosage forms with the PPI such that the second dose is higher than the first dose of the PPI.

[100] Interpreting the first and second dose to refer to amounts of drug that are loaded into the dosage form also accords with the reference in the claim to the second dose *containing* at least 10% more of the PPI than the first dose and the first and second dose independently comprising a quantifiable amount of PPI between 5 and 300 mg. These latter elements require quantification of the dose amounts before release and correspond with the teaching of the patent that the increased second dose is reflected in the total drug loading (916 Patent, Ex1, 13:1-2).

[101] While not consistent with his first report, Dr. Timko expressed the same interpretation as Apotex' experts in his second report, stating that the dosage form of the patent "contains two dose amounts and that the second dose is greater than the first" (Timko, Ex11, para 92). Although Dr. Timko attempted to resile from this statement on cross-examination, he employed an approach consistent with the statement when he later calculated the dose amount in the two pulses released from DEXILANT® using the amount of drug loaded into the dosage form for the two different bead types.

[102] When taken to the patent, Dr. Armstrong similarly conceded that the description of the first and second dose was "consistent with the dosages being contained in the dosage form" (TT 8A, 971:15-18) and that the reference in the claim to the second dose containing at least 10% more of the PPI than the first dose made clear that "dose" was referring to an amount of medicament contained in the dosage form before administration (TT 8A, 968:9-971:18).

[103] As conceded by Apotex, such interpretation of "a first and a second dose" does not import any specific formulation design. While the first and second dose may be contained within

the dosage form as two distinct populations of delayed release beads or granules as in DEXILANT®, there is no requirement for the first and second dose to be present in the dosage form as two discrete populations. Indeed, the 916 Patent is clear that the invention is not limited to a particular type of dosage form and that multiple formulation configurations are suitable for pulsed release dosage formulations (916 Patent, Ex1, 3:9-14, 10:24).

[104] I agree with Apotex, the amount of drug released from the dosage form cannot be divorced from the amount of drug (or dose) loaded into the dosage form; otherwise, there would be no certainty as to the dose amount. It would be site specific, and subject to variation from food effects and as between individuals. If the first dose and the second dose were intended to be something different from the amount of drug loaded into the dosage form, it could only be determined after the patient consumed the dosage form and then had their blood drawn and analyzed. In my view, the direct targeting of a dosage form that can provide a specific threshold plasma concentration and a second dose that contains at least 10% more PPI than the first dose runs contrary to this alternative interpretation.

(b) *"threshold concentration"*

[105] The second term in dispute is "threshold concentration". Apotex gives a plain meaning to this phrase, asserting that it refers to the plasma concentration level that must be surpassed when the dosage form is administered. It argues that "threshold" describes a limit or target, and has the same meaning as it would in common usage.

[106] Takeda asserts that “threshold concentration” is the concentration of PPI required to have an effect on a human’s gastric pH. As argued by Takeda, the use of the term “threshold” is purposive and must be read in context. As used in claim 1, it must mean something more than a concentration above at least 100 ng/mL; otherwise, it would have no additional meaning over plasma concentration in the cited phrase. Takeda asserts that when read within the context of the 916 Patent as a whole and its teachings, including Example 1, it is clear that the plasma concentration level of 100 ng/mL is the concentration above which a pharmacological effect is achieved (*i.e.*, an effect on gastric pH). Thus, the PSA would attribute “threshold concentration” to take on this meaning.

[107] While I agree that the word “threshold” indicates a target concentration for achieving pharmacological effect, I do not agree that any specific effect can be attributed to this phrase. As noted earlier, a word used in the claims can only have one and the same meaning: *Nova Chemicals* at para 82. Thus, the same meaning for “threshold concentration” must apply not only to claim 1 of the 916 Patent, but also to claims 5, 10 and 11. Claim 10 refers to “the first and second dose compris[ing] a sufficient amount of the PPI to raise plasma levels of the PPI to a threshold concentration of at least 200 ng/mL” while claim 11 provides that “the first and second dose comprise a sufficient amount of the PPI to raise plasma levels of the PPI to a threshold concentration of at least 450 ng/mL.”

[108] On cross-examination, it was shown that Dr. Armstrong adapted and adjusted his interpretation of “threshold concentration” as between the claims to match his interpretation of Example 1 and Figure 1 of the 916 Patent. For claim 1, he viewed the “threshold concentration”

of 100 ng/mL to "align with the baseline concentration that must be met to achieve an effect on the patient's gastric pH". For claim 10, he viewed the "threshold concentration" of 200 ng/mL to correlate with the point on the curve of Figure 1 where there was a high slope, "meaning small changes in plasma PPI concentration have a large resulting effect on gastric pH". For claim 11, he noted that 450 ng/mL in Example 1 was identified as the point where the effect on gastric pH had plateaued. He interpreted achieving a concentration of 450 ng/mL as ensuring that "a maximal effect on gastric pH has been achieved" (Armstrong, Ex46, para 37). Ultimately, Dr. Armstrong acknowledged that his interpretation of "threshold concentration" was subjective and based on his interpretation of Example 1 and Figure 1 of the 916 Patent (TT 8A, 988:16-998:19). It did not provide for one and the same meaning in accordance with the principles of claim construction.

[109] In contrast to Dr. Armstrong, each of Apotex' experts and Dr. Timko viewed "threshold concentration" as indicating a plasma concentration that had to be exceeded by administration of the dosage form and release of the first and the second dose of PPI. While, the experts viewed the "threshold" as indicating a target to achieve pharmacological effect (TT 1A, 111:28-112:6; TT 3A, 136:21-24; TT 5A, 541:28-544:9), the specific pharmacological effect was not part of the claim (TT 6A, 709:18-27). I view this to be a reasonable interpretation that corresponds with how the term was intended to be used by the inventors throughout the claims. It is consistent with the language of the claims, which do not refer to any particular therapeutic effect or use of the dosage form at the given plasma concentrations. It is also consistent with the language of the disclosure which refers to the threshold concentration as the concentration "above which a PPI is effective" (916 Patent, Ex1, 14:13-14) and specifically refers to the threshold concentration that

must be surpassed in a second dose of the PPI for a pulsatile release dosage form before a therapeutic effect is achieved (916 Patent, Ex1, 2a:14-15).

(c) *in humans*

[110] Takeda asserts that the plasma concentrations recited in the claims must be understood to refer to plasma concentrations in humans. It relies on Example 1 as contextualizing the language of the claims to humans rather than treating them as being open-ended and applying to both humans and animals, or mammals more broadly.

[111] Apotex asserts that a restriction to humans cannot be read into the claims where no such restriction is recited, particularly as the 916 Patent teaches that "dosage forms formulated according to the ...invention can be tested empirically in animal and/or human models to determine the appropriate PK parameters resulting from a given formulation." (916 Patent, Ex1, 13:27-29). Apotex highlights that this non-restricted interpretation is consistent with the interpretation taken by its experts and by Dr. Timko. It further relies on the decision in *Biogen* as support for its argument.

[112] In *Biogen*, the FCA found that despite the examples in the patent being limited to testing in humans it did not detract from the application of the claim to animals, particularly as the terms "patient" and "subject" as used in the asserted claims were defined to include all animals and not just humans. As stated at paragraph 97 of *Biogen*:

> [97] First, the terms "patient" and "subject", which are used in all the asserted claims, is defined to include all animals, including humans (277 Patent at para. 0037). It is clear from paragraph 007 that animals can naturally suffer from spinal cord injuries or

> diseases. It may well be that this definition could not have been appropriate if the subject matter claimed is MS only, because such disease only affects humans. Still, I find it somewhat surprising that no explanation was given, especially as Dr. Leist who insists that a subjective assessment be the subject in need of treatment is an essential element of the subject matter claimed. Obviously, if other primates are included, one could hardly require a subjective assessment. I note that the fact that the inventors tested humans only in the Examples sections would not likely be a proper explanation to disregard an express definition. Examples do not define the parameters of the claims.

[113] In this case, there is no term used in the claims with a definition that makes clear that the dosage form of claim 1 applies to both humans and animals. To the contrary, while the 916 Patent teaches that dosage forms formulated according to the invention can be tested empirically in animal or human models to determine the appropriate PK parameters resulting from a given formulation, there is no dispute that the only examples in the patent relate to human studies and that the numbers set out in the claims are derived from the human studies conducted in the patent.

[114] As acknowledged by Dr. Rowlings, the patent does not offer any information on the site of absorption or relative bioavailability in any non-humans (TT 4A, 375:27-376:2) and within mammals, human and animal gastrointestinal physiology can vary (TT 4A, 376:3-8). Similarly, the patent does not provide any information as to a target plasma concentration in any mammal, other than humans.

[115] While the PSA would expect that a pulsatile dosage form could be made to treat animals, they would know that the PK values for a dosage form for animals may be different (TT 8A, 982:20-983:4; TT 7A, 782:3-783:3; Martinez, Ex37, page 606; TT 4A, 388:21-27; TT 8A,

946:4-7). In my view, the PSA would not read the parameters set out in the claims as being anything other than human data. I agree with Takeda that while the teachings of the invention may extend to animals, the dosage form claimed would be interpreted by the PSA as being a dosage form for humans.

VII. Infringement

[116] To establish that there is infringement, the Court must be satisfied that the Apotex Product has all of the essential elements of the Asserted Claims: *Free World Trust* at para 31(f). The burden of proof lies with Takeda to establish infringement on a balance of probabilities. The evidence adduced must be "sufficiently clear, convincing and cogent to satisfy the balance of probabilities test": *Angelcare Canada Inc v Munchkin, Inc*, 2022 FC 507 at para 155, citing *FH v McDougall*, 2008 SCC 53, [2008] 2 SCR 41 at para 46; *Canada (Attorney General) v Fairmont Hotels Inc*, 2016 SCC 56, [2016] 2 SCR 720 at para 36. Evidence that estimates or speculates as to there being a possibility of infringement, however strong, is not enough: *Novopharm Ltd v Pfizer Canada Inc*, 2005 FCA 270 at para 22.

[117] In this case, I agree with Apotex, Takeda has not met this standard of proof and accordingly has not satisfied their burden. Both the formulation details and the functional data demonstrates a product that is designed for continuous release and that exhibits a single delayed release profile on dissolution *in vitro* and when examined in bioequivalence studies. The Apotex Product is not a dosage form with a first and a second dose that has pulsatile release.

A. *The Apotex Product formulation*

[118] Both the 30 mg and 60 mg dosage forms of the Apotex Product are capsules filled with the same, identical mini-tablets, [redacted] There are [redacted] mini-tablets in the 30 mg dosage form and [redacted] mini-tablets in the 60 mg dosage form. The composition of the capsules and the mini-tablets are not in dispute.

[119] Characteristic of a single continuous, delayed release dosage form, each of the mini-tablets in the Apotex Product are identical and have a [redacted] and an enteric coating that [redacted] hydroxypropyl methylcellulose 2910 ES [HPMC] and hydroxypropyl cellulose Type-LF [HPC] as [redacted] and polyethylene glycol 8000 [PEG] [redacted].

[120] While Dr. Timko opined that the [redacted] plays a functional role by impacting drug release, this position was not pursued in final argument by Takeda. The Apotex formulation documents are consistent with the evidence of Dr. Rowlings that the [redacted] is non-functional. Indeed, all of the Apotex production documents refer to the [redacted] as being non-functional. This non-functional role of the [redacted] is further demonstrated through dissolution study reports which show the dissolution profile [redacted]. As explained by Dr. Rowlings, the purpose of the [redacted]. It plays no role in the release of the drug (Rowlings, Ex25, paras

28-31). This was shown in figures 24 and 25 of Apotex' Pharmaceutical Development Report (Rowlings, Ex25, Sch 1-2:96, 99):

[IMAGES REDACTED]

[121] The enteric coating for the Apotex Product is comprised of a [redacted] It was undisputed by the

experts that on their own, these [redacted].

[122] However, there was debate between Dr. Timko and Dr. Rowlings as to the impact on dissolution of [redacted] to create the enteric coating. While Dr. Timko opined that the [redacted] enteric coating, facilitating two separate releases of dexlansoprazole, he could not support this opinion with any literature references or with any information from Apotex' regulatory documents (TT 2A, 173:27-175:15; TT 2B, 133:1-9). Nor could he explain his opinion against the information [redacted] from the [redacted] manufacturer. The [redacted] Information Guide referenced by Dr. Rowlings indicated a different dissolution behaviour when the [redacted] were combined. The [redacted] Information Guide explained that [redacted]. This explanation was also supported by the scientific literature ([redacted]).

[123] As explained by Dr. Rowlings, [redacted]

[redacted] (Rowlings, Ex25, para 56; TT 3B, 184:5-14).

[124] When challenged on cross-examination, Dr. Rowlings elaborated further, explaining how the [redacted]. As he explained, the dissolution is continuous and uninterrupted and targeted at the pH trigger.

[125] This explanation was consistent with the known functioning of the [redacted] delayed release Type II beads in DEXILANT®, which are comprised of [redacted] (TT 2A, 169:7-10). The DEXILANT® Type II beads were acknowledged by Dr. Timko as showing a target pH release point [redacted] (TT 2A, 172:3-27; 173:13-16).

B. *Dissolution Testing*

[126] The dissolution testing of the Apotex Product was also consistent with a single continuous, delayed release formulation. As shown below and explained by Dr. Rowlings, in buffered solution, the release of dexlansoprazole from both the 30 mg and 60 mg capsules began [redacted] (Rowlings, Ex25, para 78). This could be contrasted to the two stages of release arising from the dissolution of DEXILANT® in the same buffered solution. This was

shown in figures 45 and 46 of Apotex' Pharmaceutical Development Report (Rowlings, Ex25, Sch 1-2:152, 153):

[IMAGES REDACTED]

[127] Dissolution testing of the 60 mg Apo-dexlansoprazole capsules also showed an increasing rate of release of dexlansoprazole as [redacted] This was shown in figure 2 of Apotex' Dissolution Test Method Development report (Davies, Ex33, Sch 2-7:7):

[IMAGE REDACTED]

[128] While Dr. Timko and Takeda sought to assert that this [redacted] neither Dr. Rowlings nor Dr. Davies took this view and I did not find Takeda's argument or Dr. Timko's evidence on this issue compelling. A more logical explanation was provided by Dr. Davies who attributed the weak dissolution [redacted] after 7 hours to the eventual breakdown of the dosage form in the dissolution medium (TT 7B, 290:18-291:7). As noted by

Dr. Davies, the eventual dissolution at [redacted] remained consistent with a continuous release profile. None of the profiles showed release of dexlansoprazole, followed by a period of no release, and then a restart of the release, which would have been characteristic of a pulsed release dosage form as shown by the DEXILANT® dissolution profile.

C. *Bioequivalence Testing*

[129] The bioequivalence testing of the Apotex Product similarly showed data that was consistent with a continuous, delayed release dosage form. The Apotex documents provided data from [redacted]. The distribution curves for the average, mean plasma concentration-time profiles for each of the fasted studies showed a single continuous delayed release profile for the Apotex Product as compared to the two release profiles exhibited by DEXILANT® (Rowlings, Ex25, paras 92-93, 108; Davies Ex33, paras 29-33, 49-50). Similarly, a single, delayed release PK profile was also demonstrated for the Apotex Product in the average, mean plasma concentration-time profile for the fed study (Rowlings, Ex25, paras 96-97; Davies, Ex33, paras 36-38). [redacted] (Davies, Ex33, Sch 1-7:1),

[redacted]

[IMAGES REDACTED]

[IMAGE REDACTED]

[130] Both Dr. Rowlings and Dr. Davies observed that the vast majority of the individual subject profiles demonstrated the same difference in PK profile as between the two products as was seen in the mean plasma data, with the Apotex Product showing a single, continuous delayed release profile and DEXILANT® exhibiting two periods of drug release, with a shorter lag period and appreciable plasma levels starting several hours ahead of the Apotex Product.

[131] While Dr. Timko sought to point to certain of the individual bioequivalence testing to support his theory of infringement, the approach taken by Dr. Timko to the evidence had several significant flaws.

[132] First, the manner in which Dr. Timko identified plasma concentration curves of interest was not consistent. While Dr. Timko suggested that he had identified certain plasma curves that showed two drug concentration peaks (or release pulses), the criteria for concluding that two peaks existed was entirely subjective and did not account for the possibility that multiple peaks or shoulders could be caused by other factors, such as variation in absorption, metabolism, gastric emptying, or food effects, none of which are attributable to release mechanism (Rowlings, Ex25, paras 179-181, 202, 207; Davies, Ex32, para 154; Davies Ex33, paras 126, 130).

[133] Second, Dr. Timko's approach was not representative of the whole of the data and involved cherry-picking only 13 plasma concentration curves from the fasted study [redacted] from the 76 individuals tested, and only 5 plasma concentration curves from the fed study [redacted] of the 40 individuals tested there, while also downplaying the mean data.

[134] While Takeda argues that there is no need to show infringement in all instances, as infringement can be established even if other non-infringing circumstances exist (*Teva Canada Limited v Janssen Inc*, 2023 FCA 68 at para 76-79; aff'g *Janssen Inc v Teva Canada Ltd*, 2020 FC 593 at para 272), I do not find this explanation compelling here. There is no evidence to suggest that a delayed release dosage form can function as a pulsatile release dosage form in different patients. Further, even if some variability between patients could be accepted as being reflected in the bioavailability data, Dr. Timko has not sufficiently explained this. Nor has he explained the variability within the data for the same patient who received the Apotex Product twice, instead relying on only one of the two profiles for that patient to suggest two-pulse

release. He did not consider whether lack of consistency within a single patient could be the result of multiple peaking caused by other factors such as those mentioned earlier.

[135] Overall, Dr. Timko chose to focus on only a few select plasma concentration curves where he asserted there was a second peak, without effectively considering the mean data. As highlighted by Dr. Rowlings, the approach taken by Dr. Timko runs contrary to scientific principles (Rowlings, Ex25, para 215):

> 215. Average, or mean, values are calculated and relied on in science because the variability individual data points can create "artifacts", *i.e.*, apparent trends or phenomena that are entirely due to randomness and chance in the observed data. Using mean values allows a scientist to understand the "real" behaviour, which can be obscured by focussing on individual data points – this reality is essentially the opposite of Dr. Timko's opinion that the average values obscure what may have occurred in the individual subjects.

[136] Third, Dr. Timko could only estimate or approximate dose amounts for each of the perceived pulses of dexlansoprazole from the select individual plasma curves identified.

[137] As set out earlier, to arrive at the dose amounts for each of the proposed pulses, Dr. Timko drew a vertical line at the perceived low point between the two alleged pulses on the PK profile, he then determined a partial AUC for each alleged pulse as a percentage of the total AUC, and then multiplied that by 60 mg of dexlansoprazole. The approach was admittedly subjective and sought to adapt known techniques for determining AUC to the calculation of dose. It was significantly challenged on cross-examination and through the testimony of Dr. Rowlings and Dr. Davies.

[138] Both Dr. Rowlings and Dr. Davies considered the approach for identifying the two alleged doses to be speculative and to lack consideration for important kinetic principles relating to drug absorption and elimination.

[139] As highlighted in the following paragraphs from Dr. Rowlings' expert report (Rowlings, Ex25, paras 233-234) with reference to Dr. Timko's analysis of a subject from the [redacted] study (also discussed at TT 3B: 208:3-209:3):

[IMAGE REDACTED]

> 233. The first error in Dr. Timko's approach is the line he drew between the blue and green areas of the above curve .... Dr. Timko has drawn a straight line directly down from the data point for the dexlansoprazole plasma concentration recorded at [redacted] to the x-axis, as a demarcation between dose one and dose two. In doing so, Dr. Timko has chosen an artificial cut-off point between what he describes as two doses, which has no relationship to the real-life absorption of dexlansoprazole from the Apotex Product that occurred in this subject.
>
> 234. Dr. Timko marks the [redacted] point in the study as a point in time where the first dose of dexlansoprazole is entirely absorbed into the plasma, and the absorption of the second dose of dexlansoprazole has not yet begun, such that the entire area under

> the curve to the left of that point can be assigned to dose one, and the entire area under the curve to the right of that point can be assigned to dose two. However, even if there were two doses released from the Apotex Product and then absorbed into the plasma .... there is no time-point where the entirety of dose one has been absorbed, and eliminated, and then the absorption of dose two begins. The suggestion of an arbitrary and instantaneous cut-off defining one portion of dose being completely absorbed and immediately afterwards having absorption start form the second portion of dose is not consistent with known timeframes for release from a dosage form and absorption processes.

[140] As explained by Dr. Davies (Davies, Ex33, para 136), taking the low point between the two asserted “peaks” as the separation point, does not take into consideration how absorption and elimination works. It implies that at that point in time the first dose has already been released from the dosage form, absorbed into the systemic circulation, and into the individual’s plasma, and then is instantaneously eliminated. It similarly implies that at the same moment, the second dose is also released from the dosage form, absorbed into the systemic circulation, and into the individual’s plasma, and then is instantaneously raising the drug plasma concentration.

[141] To estimate dose amounts in this manner, the portions of the plasma curves attributable to each of the two peaks need to be separated by taking into consideration the absorption, distribution, metabolism and excretion of dexlansoprazole, which would involve knowing the elimination rate constant for the first portion and the absorption rate constant for the second portion (Davies, Ex33, para 142).

[142] Even then the dose amounts were derived from plasma concentration data and do not correlate with the amount of drug/dose loaded into the dosage form and released upon administration. In addition to the dose calculation being an estimation, it was also based on an

assumption that the AUC could be normalized to the 60 mg dose amount, without considering the likelihood of variable and incomplete oral bioavailability (Rowlings, Ex25, paras 236-237; Davies, Ex33, paras 155-156).

[143] Further, even if this approach could be taken, as admitted by Dr. Timko, the AUC determination was not estimated based on the total drug absorbed, which meant that exposure levels for the first perceived dose were likely lower than what was calculated, and that the exposure levels for the second perceived dose were likely higher (TT 2B, 111:13-115:23). Dr. Timko acknowledged that if the dose amounts were estimated based on consideration for the total drug absorbed that his dose amounts would have included estimated first dose amounts for at least some of the subjects of less than 5 mg.

[144] The inaccuracies with the approach taken by Dr. Timko were further illustrated in calculations made on plasma concentrations curves for DEXILANT®. When Dr. Rowlings attempted to use Dr. Timko's approach to estimate the partial AUCs from profiles for some of the same individuals who were also administered DEXILANT®, the first dose and the second dose amounts varied across individuals and did not match the actual amounts reported to be included in the two doses amounts (TT 2A, 186:23-187:16; Rowlings, Ex25, paras 247-250). While I accept that this analysis was done with subjects in the fed study (TT 4B, 251:27-253:15), which may have made the analysis more difficult, in my view it still serves to highlight the variability and complications with Dr. Timko's approach.

[145] Although Apotex raised additional criticisms with Dr. Timko's analysis, in my view the flaws noted above were sufficient to raise significant doubts with respect to the approach taken by Dr. Timko to attempt to identify and calculate a first dose and a second dose amount from the plasma concentration-time profiles.

D. *Conclusion on Infringement*

[146] Upon considering the evidence relating to the Apotex Product design, the dissolution testing, and bioequivalence testing, it is my view that Takeda has not satisfied their burden of establishing infringement.

[147] Takeda has not established that there is a first and a second dose of dexlansoprazole in the dosage form and accordingly released from the dosage form as two discrete pulses. Nor has it been shown for the same reason that there is a second dose of dexlansoprazole that contains at least 10% more dexlansoprazole than the first dose, or that there are first and second dose amounts between 5 and 300 mg. Rather, the evidence indicates that there is only one dose of dexlansoprazole in each 30 mg or 60 mg capsule of the Apotex Product that is released from the Apotex Product in a single, continuous delayed release fashion. The essential elements of the Asserted Claims have not been met.

[148] Although this finding on infringement is sufficient to dispose of the entirety of the action, I will go on to consider the invalidity arguments that have been raised, which formed a significant portion of the parties' arguments at trial.

VIII. Validity

[149] Subsection 43(2) of the *Patent Act* states that a patent is presumed to be valid in the absence of evidence to the contrary. The presumption is rebutted if the evidentiary record contains any evidence which, if accepted, is capable of supporting the grounds of invalidity claimed: *Abbott v Canada (Health)*, 2007 FCA 153 at para 10. Once the presumption is rebutted, the party challenging the patent bears the legal burden to prove the patent is invalid on a balance of probabilities. Thus, in this case, Apotex bears the legal burden to prove the patent is invalid for one or more of the grounds of anticipation, obviousness, inutility, insufficiency, overbreadth, ambiguity, and as unpatentable subject-matter.

A. *Anticipation*

[150] The proposed invention claimed in a patent must be new to be patentable. Subsection 28.2(1) of the *Patent Act* sets out the requirement for novelty of a patented invention. As relevant to this decision, paragraph 28.2(1)(b) of the *Patent Act* provides that the subject-matter defined by a claim must not have been disclosed before the claim date (here, June 16, 2004) by a person who was not the applicant, or 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.

[151] The Supreme Court of Canada in *Sanofi*, set out two requirements for establishing anticipation: prior disclosure and enablement. For disclosure to be satisfied, it is not necessary that “the exact invention” was made and publicly disclosed. Rather, “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": *Sanofi* at paras 23 and 25. For enablement, the PSA must have been able to perform the invention: *Sanofi* at para 26.

[152] As agreed by the parties, the debate in this case focusses on whether there was prior disclosure of the invention as claimed. To meet this requirement "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": *Sanofi* at para 25. As set out in *Gilead v Canada,* 2013 FC 1270 at paragraph 30: "[i]f there is doubt about what the prior art reference includes, it cannot be taken to meet the definition of anticipation": see also *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2016 FC 580 at para 243; aff'd 2017 FCA 76; *Sanofi* at para 21, citing *General Tire & Rubber Co v Firestone Tyre & Rubber Co*., [1972] RPC 457 at 486.

[153] It is important to highlight that disclosure may be made without any recognition of what is present or what is happening: *Abbott Laboratories v Canada (Minister of Health),* 2008 FC 1359 at para 75; aff'd 2009 FCA 94. Knowledge of a prior public disclosure is not necessary for there to be anticipation. If a skilled person practising the prior art would have made a product with the inherent attributes of subsequently claimed subject-matter, that prior art may anticipate the later claims. As reasoned in *Abbott v Canada (Minister of Health),* 2007 FCA 153 [*Abbott*] at paragraphs 18-22, the absence of knowledge of the subject-matter of the invention in such context is legally irrelevant:

> [18] In this case, the Judge found that clarithromycin Form II was known at the relevant time. That conclusion is supported by a body of evidence to the effect that the creation of a crystal form of clarithromycin by the use of solvents was known prior to July 29, 1996. I need not list all the prior art references. It is sufficient to say that the Judge understood the evidence of Dr. Myerson, a

witness for Abbott, to confirm that an article by Yoshiaki Watanabe and others, published in 1993 in *The Journal of Antibiotics*, describes substantially the same process as described in example 10 of the disclosure in the 732 patent, which is said to result in clarithromycin Form II.

[19] Abbott points out that that the Watanabe article does not state that the result of the process in the article is clarithromycin Form II. Nor is there evidence that any of the witnesses for Apotex attempted to follow the Watanabe article to see if it produced clarithromycin Form II. Because of that, it would have been open to the Judge to draw an inference adverse to Apotex on that point.

[20] However, the Judge also had before him the patent disclosure representing that the method described in example 10 results in clarithromycin Form II. There was no evidence that the representation in example 10 is false. Therefore, it was open to the Judge to infer that following substantially the same process as described in the Watanabe article would also have produced clarithromycin Form II. Given the body of evidence presented to the Judge, I cannot conclude that he made a palpable and overriding error in accepting the truth of the representation in example 10 of the patent disclosure and following its logic.

[21] The conclusion of the Judge is also supported by evidence relating to the creation of clarithromycin Form II by a heating technique that was known before 1996. Clarithromycin Form II can be obtained by heating clarithromycin Form I by that known technique until its temperature exceeds 135˚C. It is undisputed that clarithromycin Form I, when so heated, is transformed into clarithromycin Form II at some point after the heated substance reaches 135˚C, although it ceases to be clarithromycin Form II by the time the substance reaches the melting point at 225˚C.

[22] Abbott argues that a person skilled in the art who heated clarithromycin Form I by the known technique would not and could not know that clarithromycin Form II had been created, unless they also knew that the heating process had to be stopped before the substance reached its melting point at 225˚C. In my view, the absence of that knowledge is legally irrelevant. The undisputed evidence is that clarithromycin Form II would have been present if the heating technique had been followed. There were well established analytical techniques that would have disclosed its presence if anyone had cared to look at the appropriate moment.

[154] Apotex argues that the Asserted Claims are anticipated by examples 5, 6, 11 and 21 of the 574 Application. It further asserts that example 57 of the 574 Application, which discloses a formulation that is the same as DEXILANT® but for one of its excipients is also anticipatory under the principle set out in *Abbott*.

[155] As a starting point, it is important to remember that the focus of the anticipation analysis is on the essential elements of the claims in issue. Outside of selection patents, the disclosure of advantages of the subject-matter of the claims is not necessary for a finding of anticipation: *Swist v MEG Energy*, 2022 FCA 118 at paras 69-70.

[156] Dr. Armstrong was provided with legal instructions that incorrectly advised him that for anticipation "[e]very element of the claim, including its advantages, must be publically disclosed in a single document." [emphasis added] Therefore, his analysis delved into areas that were not appropriate for an anticipation analysis. This fact, combined with an admission by Dr. Armstrong that his analysis of the 574 Application relied on descriptions made by Takeda and not on any analysis that he conducted on his own (TT 8A, 1047:14-18), that the analysis he made of the examples relied on incorrect numbers as to dose (TT 8A, 1043:26-1045:16), and that he had not conducted a full review of the 574 Application examples in issue (TT 8A, 1048:9-1053:7, 1054:5-1055:11), renders his opinion on anticipation of limited assistance to the Court.

[157] Nonetheless, even without giving weight to Dr. Armstrong's evidence, the evidence put forward by Apotex must still be sufficient to establish on a balance of probabilities that the legal test for anticipation has been satisfied.

[158] By way of background, the 574 Application relates generally to "a controlled release preparation, in particular a capsule comprising a tablet, granule or fine granule wherein the release of active ingredient is controlled by a gel-forming polymer which delays the migration speed in the gastrointestinal tract" (574 Application, Ex32, Sch 6-35, 1:5-9). The 574 Application refers to optically active compounds such as the *R* and *S* enantiomers of lansoprazole as being preferred compounds. As noted by Dr. Davies, dexlansoprazole is the only active ingredient used in the preparations found in the examples, which would lead the PSA to focus on it (TT 6A, 619:22-28, 622:5-7).

[159] The 574 Application teaches that absorption of the active pharmaceutical ingredient in the pharmaceutical composition of its invention from the digestive tract "is controlled by two kind [sic] of systems utilizing (1) a release control of active ingredient by a controlled release tablet, granule or fine granule and (2) retentive prolongation in the digestive tract of a tablet, granule or fine granule by a gel-forming polymer, or their combinations" (574 Application, Ex32, Sch 6-35, 16:19-23). The release active ingredient can occur continuously or "in a pulsatile manner from the tablet, granule or fine granule" to allow for "prolonged absorption and drug efficacy" (574 Application, Ex32, Sch 6-35, 17:6-9). I accept the evidence of Dr. Davies that the efficacy of a PPI would be understood to mean raising gastric pH for increased efficacy in the treatment of acid-related GI disorders (Davies, Ex32, para 267).

[160] For pulsatile release formulations, the 574 Application indicates that capsules may be prepared without a gel-forming polymer, and may be prepared "by combining the release-controlled tablet, granule or fine granule with a fast-releasing type granule having only enteric

coat" (574 Application, Ex32, Sch 6-35, 114:25-115:2). Such preparation can have a blood level that "is preferably enhanced at a more earlier stage to achieve drug efficacy and to reach the first maximal blood level, and then the second maximal blood level is reached by the release of active ingredient from granules in which the release was controlled, that is, two peaks are expressed" (574 Application, Ex32, Sch 6-35, 115:5-10).

[161] It is undisputed that each of examples 5, 6, 11 and 21 of the 574 Application teach capsules that contain two types of dexlansoprazole-containing granules that provide for pulsed release at different sites in the GI tract. The pharmacokinetics of the capsules were tested in beagle dogs, and reached C_{max} values of between 186-657 ng/mL. However, they were not tested in humans.

[162] While Dr. Davies and Dr. Rowlings each gave evidence that the quantities of dexlansoprazole in each of the doses in the pulsed release capsules of examples 5, 6 and 21 were between 5 and 300 mg, with the second dose being at least 10% greater than the first dose, when asked about these calculations on cross-examination Dr. Rowlings readily admitted that an error had been made in his calculation of the first dose amounts. The reference examples that had to be used to calculate the first dose amount stated that "[t]wo ... capsules ... were filled with the resulting mixture to obtain a capsule" (574 Application, Ex32, Sch 6-35, 317:2-4, 10-12; 329:8-10); thus, providing for a mixture that was for two capsules, not one capsule, as calculated by Dr. Rowlings. Therefore, it was revealed that Dr. Rowlings' dose amount number should have been divided by two, such that the amount of dexlansoprazole in the first dose for each of

examples 5, 6 and 21 was 4.25 mg instead of 8.5 mg as Dr. Rowlings reported (TT 4A, 395:11-396:11; 397:20-399:11).

[163] Dr. Davies arrived at the same numbers as Dr. Rowlings, but disagreed that the examples made two capsules, instead insisting that the 8.5 mg number was correct, focussing only on the last part of the quoted statement "....to obtain a capsule", while ignoring its preceding reference to two capsules and the total amount of the mixture (809 mg) which, as admitted by Dr. Rowlings, was objectively too large for single capsule preparation (TT 4A, 394:17-20). In my view, this is not a reasonable reading of the text of the 574 Application. I agree with Takeda it is clear from the 574 Application that the resulting mixture was not filled into one capsule.

[164] As admitted by Apotex, if examples 5, 6 and 21 have a first dose of 4.25 mg instead of 8.5 mg, these examples do not anticipate the Asserted Claims. I similarly find that examples 5, 6 and 21 are not anticipatory for at least this reason.

[165] Example 11 was different than examples 5, 6 and 21, and resulted in a mixture of 30 mg dexlansoprazole which filled one capsule only. The calculations conducted by Dr. Rowlings and Dr. Davies resulted in dose amounts of 7.1 mg and 21.4 mg for the first and the second dose respectively, which admittedly did not add up to 30 mg. While both experts suggested that 30 mg was a "target" or estimate only, and that it was not necessary for the dose amounts to add up to 30 mg, it was shown on cross-examination that if Dr. Rowlings and Dr. Davies had calculated the dose amounts differently, and in a manner consistent with how they calculated the dose amounts for other examples, the dose amounts for the first and the second dose would have been

different, *albeit* within the 5 to 300 mg range provided by claim 1. If calculated in a consistent manner, the second dose, however, would not have been at least 200% higher than the first dose as required by claim 8 of the 916 Patent (TT 6A, 734:26-735:9).

[166] Moreover, irrespective of these dose calculations, each of examples 5, 6, 11 and 21 did not disclose a threshold plasma concentration of 100 ng/mL. First, there was no disclosure of any plasma concentration being a threshold which must be surpassed for pharmacological effect and second, the only plasma concentrations disclosed were those relating to studies in beagle dogs.

[167] Dr. Davies suggested that the studies in beagle dogs were “translatable” to humans. However, there was no information in the 574 Application to support this suggestion and I do not accept that this can be taken as part of the CGK. Rather, the CGK was that humans and dogs have different gastro-physiology and that a PSA would have to test both species to determine if the plasma concentrations were the same (TT 7A, 782:20-783:3). Further, there was no information in the 574 Application on how or whether the plasma concentrations measured in dogs would have had any pharmacological effect in dogs, or humans, as only the PK values were measured. The 100 ng/mL was not disclosed as a threshold concentration that needed to be surpassed. As such, I agree with Takeda, example 11 does not anticipate the Asserted Claims and examples 5, 6 and 21 are not anticipated for this additional reason.

[168] This leaves example 57. This example is different from examples 5, 6, 11 and 21 as it does not include any PK data of any kind resulting from administration of the capsule. For this

example, Apotex relies on *Abbott*. It highlights that example 57 provides a formulation that is close to DEXILANT® except that it includes the excipient PEG as part of the formulation.

[169] Apotex relies on data from Takeda's clinical trials CPH-502 and RCP-0023 which showed that dosage forms TAK-390MR-E and TAK-390MR 3 (that are for the same formulation as example 57, aside from the use of PEG as a plasticizer) reached plasma concentrations in humans of 700-800 ng/mL for the first pulsatile release and 1100-1200 ng/mL for the second pulsatile release (Davies, Ex32, paras 339-341).

[170] Both Dr. Rowlings and Dr. Davies testified that the addition of PEG as a plasticizer in the enteric coating layer of the granules of a preparation with the formulation details of example 57 would not influence the pharmacokinetics of the capsules. This point was not undermined on cross-examination and no expert gave contradictory evidence.

[171] Apotex asserts that the circumstance of this case aligns with *Abbott*, in that the disclosure of a formulation equivalent to that of DEXILANT® is disclosure of the PK properties that would be achieved from the formulation on its administration. It asserts that these properties were inherent in the dosage form even if unrecognized at the time of the 574 Application.

[172] Takeda contends that the Asserted Claims are not inherently anticipated by example 57. It raises several concerns with Apotex' argument. Of most significance, it asserts that example 57 is not akin to the situation in *Abbott*.

[173] Takeda relies on two primary decisions in support of its argument, both of which are in a selection patent context: *Novo Nordisk Canada Inc v Cobalt Pharmaceuticals Inc*, 2010 FC 746 [*Novo Nordisk*] and *Allergan Inc v Apotex Inc*, 2022 FC 260 [*Allergan*].

[174] In *Novo Nordisk*, the patent in dispute (851 Patent) claimed the *S*-enantiomer of a compound (repaglinide), its use for the treatment of Type 2 diabetes, and a process to make it. Cobalt asserted anticipation by a prior genus patent (398 Patent) that disclosed over a million compounds that included repaglinide and its enantiomers, and an application (331 Application) that claimed two new solid forms of the racemate, its enantiomers and salts and their use for the treatment of Type 2 diabetes. In rejecting Cobalt's inherent anticipation argument, the Court noted that although the racemate of repaglinide had been synthesized at the time of the prior art, repaglinide itself had not been made, let alone tested. Neither its absolute configuration nor its special PK advantages were known. Moreover, no preference was expressed in the 398 Patent for the use of the *S*-enantiomer over the *R*- enantiomer or its racemate. The comments at paragraphs 170-174 are of particular note:

> [170] Indeed, Cobalt acknowledges that nothing in the '398 patent discloses repaglinide's allegedly special pharmacokinetic advantages. Cobalt contends, however, that if repaglinide's pharmacokinetic properties are considered to be inherent in the claims of the '851 patent, then they would also be inherent in the compounds claimed by both the '398 patent, and, particularly, by the '331 patent application, with the result that the invention claimed by the '851 patent was anticipated. I do not accept this submission.
>
> [171] There is no disclosure in either the '398 patent or the '331 patent application that defines in clear terms the nature of the pharmacokinetic advantages allegedly possessed by repaglinide. Simply claiming the 388 compound and its enantiomers does not mean that those properties are included in the prior patents.

> [172] Indeed, the same argument could have been advanced by the generic in the *Sanofi* case. There, the assertion was that the dextro-rotatory isomer was less toxic and better tolerated than either the levo-rotatory isomer or the racemate. Those advantages would be inherent properties of the dextro-rotatory isomer, and thus would have been present, if unrecognized, in the compounds claimed in the genus patent. Nevertheless, the Supreme Court found that the invention claimed in the patent in issue had not been anticipated by the prior genus patent.
>
> [173] The ’331 patent application claims solid forms of the racemate of repaglinide together with its (S) and (R) enantiomers. Once again, the absolute configuration of repaglinide is not disclosed in the ’331 patent application, and Cobalt concedes that repaglinide’s alleged special pharmacokinetic advantages are also not disclosed.
>
> [174] Indeed, it is clear from the evidence that one cannot predict the relative activity and pharmacokinetic properties of enantiomers without actually separating and testing them. The ’331 patent application only discloses testing of the racemate Furthermore, the only testing of the racemate that was carried out was in relation to hypoglycemic activity and acute toxicity. There is no indication in the ’331 patent application that the enantiomers were tested at all, nor is any preference expressed for the (S) enantiomer over either the (R) enantiomer or the racemate.

[175] In *Allergan*, the Court similarly rejected an inherent anticipation argument made on the basis of a prior patent application (BR 601) that included within its scope the formulation of the patent at issue on the basis that it did not disclose the PK properties (food effect) of the invention:

> [367] ... BR 601 was not about the food effect and did not disclose that pharmaceutically effective absorption would be achieved if its formulations were taken with or without food. Without such disclosure, even if the skilled person read BR 601 and chose exactly all the essential elements in the precise amounts disclosed in the ‘188 Patent (which would require significant trial and error) and arrived at some formulation of the ‘188 Patent, the lack of disclosure in BR 601 of the inherent properties dictates against finding that BR 601 anticipates the ‘188 Patent (*Novo Nordsik*). BR 601 makes no mention of administration in the fed or fasted state or pharmaceutically effective absorption.

[176] While the 916 Patent is not a selection patent, the heart of the invention of the 916 Patent is the recognition of the threshold plasma concentration and how to achieve and maintain it (*i.e.*, with a pulsatile release dosage form that has a second dose that is at least 10% greater than the first dose). There was no suggestion in the 574 Application of any recognition of these properties, nor of their significance. Further, there was no disclosure of administration of the capsule formulation of example 57 within the 574 Application.

[177] Thus, unlike in *Abbott* where it was inevitable that the compound was made through the Watanabe processing steps and would have resulted in the formation of Form II clarithromycin, to arrive at the threshold concentration here, the capsules of example 57 would have had to be administered to humans and the PK properties would have to be identified and studied. These steps were not disclosed in the 574 Application and are not, in my view, inherent simply from the preparation of the capsules themselves. In my view, it cannot be said that example 57 of the 574 Application inherently discloses all essential elements of the Asserted Claims.

B. *Obviousness*

(1) Legal Principles

[178] Section 28.3 of the *Patent Act* provides that the subject-matter of a claim in an application for a patent must be subject-matter that would not have been obvious on the claim date to the PSA, having regard to information that was made available to the public: (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; and, (b) before the claim date, by a person not mentioned in (a). Obviousness is a difficult test to satisfy because it necessitates showing that

the PSA would have come directly and without difficulty to the invention, without the benefit of hindsight: *Bridgeview Manufacturing Inc v 931409 Alberta Ltd (Central Alberta Hay Centre)*, 2010 FCA 188 [*Bridgeview*] at para 50.

[179] The Supreme Court of Canada in *Sanofi* set out a four-step approach to the obviousness analysis at paragraph 67 of its decision, as follows:

> (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?

[180] It was recognized in *Sanofi* that for areas of endeavour where advances are often won by experimentation, an "obvious to try" analysis may be appropriate to take into consideration at the fourth step of the obviousness inquiry. The critical question is whether it "was more or less self-evident to try to obtain the invention" having regard to the following non-exhaustive factors, while noting that "[m]ere possibility that something might turn up is not enough" (*Sanofi* at paras 66, 68-69):

> 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?

[181] The Court must be cautious, however, when approaching the obvious to try analysis as it remains as only one factor amongst many that may assist in the obviousness inquiry: *Bristol Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76 [*Atazanavir*] at para 38; *Sanofi* at para 64. It is not intended to displace other tests.

[182] As the Supreme Court in *Sanofi* made clear, when considering obviousness, the Court favours "an expansive and flexible approach that would include 'any secondary considerations that [will] prove instructive'": *Sanofi* at para 63; *Atazanavir* at para 61. The analysis is to be flexible, contextual, expansive and fact-driven (*Apotex Inc v Pfizer Canada Inc*, 2019 FCA 16 at para 39) and is to be undertaken on a claim-by-claim basis (*Apotex Inc v Shire LLC*, 2021 FCA 52 at paras 26 and 55 [*Shire*]).

(2) PSA and CGK

[183] The PSA and their CGK were set out earlier at paragraphs [76] through [89] of these reasons. I adopt these same findings for the obviousness analysis.

(3) Inventive Concept

[184] There is some debate in the jurisprudence and as between the parties as to how to approach the inventive concept.

[185] Apotex argues that the inventive concept is no different than the essential elements of the claims. It argues that the comments of the FCA in *Ciba Specialty Chemicals Water Treatments Limited's v SNF Inc*, 2017 FCA 225 [*Ciba*] at paragraphs 74-77 should apply:

> [74] The reminder in *Unilever* that it is inventive concept of the claim which is in issue, "not some generalised concept to be derived from the specification as a whole," is very apt: *Unilever* at page 569. Part of the difficulty in the search for the inventive concept is the use made, or to be made of the disclosure portion of the specification of the patent. In *Connor Medsystems Inc v Angiotech Pharmaceuticals Inc* [2008] UKHL 49, [2008] R.P.C. 28 (*Connor*), Lord Hoffman wrote at paragraph 19 that "[t]he patentee is entitled to have the question of obviousness determined by reference to his claim and to some vague paraphrase based upon the extent of his disclosure in the description."
>
> [75] This emphasis on the claims is consistent with section 28.3 of the Act which stipulates that it is "the subject-matter defined by a claim" which must not be obvious.
>
> [76] Lord Jacob was alive to the possibility that difficulties in the identification of the inventive concept could lead to "unnecessary satellite debate". His counsel was that "if a disagreement about the inventive concept of a claim starts getting too involved, the sensible way to proceed is to forget it and simply to work on the features of the claim": *Pozzoli* at paragraph 19. Lord Hoffman wrote, once again in *Connor* at paragraph 20, that the inventive concept "is a distraction almost as soon as there is an argument as to what it is."
>
> [77] There may be cases in which the inventive concept can be grasped without difficulty but it appears to me that because "inventive concept" remains undefined, the search for it has brought considerable confusion into the law of obviousness. That uncertainty can be reduced by simply avoiding the inventive concept altogether and pursuing the alternate course of construing the claim. Until such time as the Supreme Court is able to develop a workable definition of the inventive concept, that appears to me to be a more useful use of the parties' and the Federal Court's time than arguing about a distraction or engaging in an unnecessary satellite debate.

[186] Takeda argues that the inventive concept should be independently determined as it is a separate part of the *Sanofi* test. It contends that Apotex' argument ignores the latest word on the inventive concept from the FCA in *Shire* where the FCA expressly stated that they disagreed that the effect of section 28.3 of the *Patent Act* was to narrow the inventive concept to the essential elements of the claims:

> [74] I cannot agree that the effect of section 28.3 of the *Patent Act* is to narrow the inventive concept to the essential elements of the claim itself. This conflates the claims construction exercise with the identification of the inventive concept, and would alter, in a very significant manner, the inquiry into "inventiveness", which is the sole purpose of the obviousness inquiry. Beyond *Sanofi*, there are many cases in which this Court has upheld the use of a specification to determine the inventive concept where it was not readily discernable from the claims themselves (*Apotex Inc*. v. *Allergan* at paragraph 72, citing *Apotex Inc. v ADIR*, 2009 FCA 222, 75 C.P.R. (4th) 443 at paragraph 58).

[187] As noted in *Shire* at paragraphs 75 and 76, while identification of the inventive concept follows from, and is informed by, claims construction, claims construction and determination of the inventive concept serve two different purposes. Claims construction occurs before any assessment of the validity of the claims; its purpose being to interpret and determine the scope of the claims by looking at its subject-matter. Identification of the inventive concept occurs within the assessment of the validity of the claims. Its purpose is to determine what, if anything, makes the claims, as construed, inventive, to facilitate the obviousness analysis (see also *Merck Sharp and Dohme Corp v Pharmascience Inc,* 2022 FC 417 [*Pharmascience*] at para 168).

[188] Takeda argues that the inventive concept is the expression of 'why' the claimed subject-matter is inventive and looks at the benefits of the invention as claimed. Although the position put forward by Takeda in final argument was not cited to any expert, it asserts that the inventive

concept of claim 1 includes: the properties of the dosage form (a dosage form that releases PPI as two pulsed doses); the determination of a threshold concentration of at least 100 ng/mL, at which point a pharmacological effect is achieved in humans; a larger second dose of PPI being released from the dosage form, including the teaching of regional PPI absorption from Example 2; and the benefits of once-daily treatment.

[189] In my view, the additional comments provided in *Shire* at paragraph 67 are instructive and serve to resolve the FCA's comments in *Shire* with those in *Ciba*. In paragraph 67, as set out below, the FCA provides further guidance on the approach to be taken when determining the inventive concept:

> [67] First, on occasion, the inventive concept may be "readily apparent" where there is agreement on it. If not, the inventive concept needs to be construed. To do that, the judge is to first determine whether it can be identified from the previously completed claim construction exercise (*Ciba*, at paragraphs 76-77). Second, where it is not possible to fully grasp the nature of the inventive concept solely from those claims, the judge may have regard to the patent specification to determine if it provides any insight or clarification into the inventive concept of the claim(s) in issue (*Sanofi*, at paragraph 77; *AstraZeneca Canada Inc*., at paragraph 31). If this step is necessary, "it is not permissible to read the specification in order to construe the [inventive concept of the] claims more narrowly or widely than the text will allow" (*Sanofi*, at paragraph 77).

[190] In this case, the inventive concept has not been agreed to by the parties. However, in my view, it is clearly grounded by the language of the claims, and emerges from the previous claims construction exercise, when considered in context with the teachings of the patent and the statement made at page 2a of the 916 Patent (cited in paragraph [14] above).

[191] The inventive concept is the same as the solution taught for overcoming nocturnal breakthrough with a PPI once daily oral dosage form. This is claimed in the Asserted Claims as a dosage form with two pulsed doses designed around the recognition that there is a threshold plasma concentration to achieve therapeutic effect. In claim 1, this is claimed as the threshold plasma concentration of at least 100 ng/mL. In claims 10 and 11, this is the threshold plasma concentrations of 200 ng/mL and 450 ng/mL, respectively. A second aspect of the inventive concept is the recognition that to maintain the threshold plasma concentration for a PPI pulsatile release dosage form, the second dose must be greater than the first dose to account for absorption differences in the GI tract. In claim 1, the second dose is at least 10% more than the first dose. In claim 6, the second dose is at least 50% more than the first dose; in claim 7, at least 100-200% more than the first dose; and in claim 8, at least 200-900% more than the first dose. As noted previously, claim 5 merely adds that the threshold plasma concentration persists for at least 30 minutes and claim 16 specifies that the PPI is the *R*-enantiomer of lansoprazole, which is dexlansoprazole.

[192] In my view, these purported inventive aspects, which are grounded in the claims of the 916 Patent, comprise the inventive concepts of the respective claims.

(4) Comments on Expert Evidence

[193] Before delving into the remaining parts of the *Sanofi* test, it is necessary to provide some additional comments on the expert evidence.

[194] First, with respect to Dr. Armstrong, there are certain limitations to his evidence that must be mentioned. As highlighted by Apotex, his mandate was restrictive. Dr. Armstrong was only asked to respond to the reports of Dr. Kahrilas and Dr. Davies. He did not respond to Dr. Rowlings. He was not asked to assess the 916 Patent, ascertain the inventive concept, and compare it to the state of the art to provide an independent opinion (TT 8A, 956:3-10); nor did he provide an obvious to try analysis. He did not engage in an exercise whereby the state of the art relied upon by Apotex was compared to the inventive concept (TT 8A, 1014:7-12). While his report necessitated a view on some of these points as part of his response to Apotex' experts, the comments made were not within the full context of an obviousness analysis.

[195] Second, Dr. Armstrong was mistakenly of the view that only CGK (instead of prior art) could be considered for the obviousness analysis and that CGK was restricted to information that did not require the PSA to take risks and was limited to only information that was a "good basis to rely upon and/or combine with other information" (Armstrong, Ex46, para 56; TT 8A, 1003:3-16). This narrowed the lens from which he considered obviousness and through which he made his comments with respect to Dr. Kahrilas' and Dr. Davies' opinions. I have therefore afforded limited weight to the comments made by Dr. Armstrong as to what constitutes the state of the art.

[196] Further, as noted earlier, Dr. Armstrong did not conduct his own review of the prior patent applications. Rather, his review of this prior art relied upon summaries provided by Takeda's counsel. Accordingly, I afford limited to no weight to the conclusions made on these references in his report. As Dr. Armstrong readily admitted to these shortcomings during testimony, and in view of his accepted expertise, I do not hold the same reservation to the

comments made on cross-examination where he was asked his opinion on specific information from the documents.

[197] On Apotex' side, I have two comments. First, both Dr. Rowlings and Dr. Kahrilas assumed that the threshold concentration claimed would not require inventive ingenuity (Rowlings, Ex24, paras 28, 403, 441; Kahrilas, Ex31, paras 26, 232). As this was a key aspect of the inventive concept this assumption, in my view, clouds the overall opinion given by these experts to whether any differences between the inventive concept and the state of the art was obvious. As highlighted by Takeda, Dr. Davies was the only expert from Apotex' side that considered all relevant aspects of the claims when conducting his analysis.

[198] Second, Apotex' experts determined whether there were differences between the prior art and the inventive concept by looking at the prior art references trying to find the individual elements of the claims (TT 5A, 573:5-28, 574:16-575:9; TT 7A, 747:13-20; TT 4A, 450:13-22). This selective approach fails to consider the references in context and is characteristic of a hindsight analysis: *Gilead Science Inc v Canada (Health0*, 2013 FC 1270 at para 37; *Janssen Inc v Teva Canada Ltd*, 2020 FC 593 at para 169; *Bridgeview* at para 51; *Zero Spill Systems (Int'l) Inc v Heide*, 2015 FCA 115 at para 95; *Corlac Inc v Weatherford Canada Inc*, 2011 FCA 228 at para 69. As such, I have approached the opinions of Apotex' witnesses as to step 3 of the *Sanofi* analysis with some caution.

(5) State of the Art and Step 3 of the *Sanofi* Analysis

[199] While step 3 of the *Sanofi* test refers to the goal posts of the comparison that is to be made as between the "state of the art" and the "inventive concept", section 28.3 of the *Patent Act* requires a comparison between the "information that was made available to the public" and the "subject-matter of the claims". As clarified in *Ciba* at paragraph 60, when taken together, this boils down to a comparison between the inventive step and the prior art, which is the prior art relied upon by the person alleging obviousness. While the prior art may be supplemented to include additional references identified by a plaintiff or art that is considered to teach away from the direction of the invention, it is not the prior art at large: *Apotex Inc v Janssen Inc*, 2021 FCA 45 at para 25; *Pharmascience* at para 160. At this stage of the analysis, it is not important to consider whether the prior art would have been located by a PSA in a reasonably diligent search, although this might come into play at step 4 of the obviousness analysis when determining whether the uninventive PSA would combine that prior art with other prior art to make the claimed invention: *Hospira FCA* at para 86.

[200] In this case, the key prior art relied upon by Apotex for the state of the art included the 574 Application, WO 97/48380 [WO 380], WO 99/32093 [WO 093], WO 777 and WO 584.

[201] Although Takeda does not dispute that these references disclose pulsed release dosage forms of PPIs with once-daily administration, or that they disclose a broad range of PPI plasma concentrations, Takeda contends that there are two differences between the state of the art and the inventive concept of the claims. First, there is no correlation between the plasma concentrations and C_{max} values disclosed in the art and the identification of a threshold

concentration that must be surpassed for pharmacological effect. Second, the prior art does not demonstrate an appreciation that the second dose released from a multi-dose dosage form must be larger than the first dose because of how a PPI is absorbed in a patient's GI tract.

[202] As set out earlier, the 574 Application taught controlled release dosage forms containing PPIs, including the *R*-enantiomer of lansoprazole, in the form of a capsule comprising a tablet, granule, or fine granule, which could be formulated as a pulsatile release formulation. The 574 Application provided 76 examples, 45 of which related to pulsatile release dosage forms of which at least 17 included second dose amounts that were greater than the first dose amount. These included examples 5, 6, 11, 21 and 57. As set out above, examples 5, 6, 11 and 21 provided PK properties for the dosage forms from studies in beagle dogs that reported peak plasma concentrations of 186 ng/mL to 657 ng/mL. As admitted by Dr. Rowlings, the 574 Application provided no preference for any particular dosage form, or for a dosage form with a second dose greater than the first dose (TT 4A, 419:11-421:19, 454:10-14).

[203] WO 380 disclosed dosage forms that extended release of the PPI for improved inhibition of gastric acid secretion and an improved therapeutic effect (Kahrilas, Ex31, paras 205, 208; Rowlings, Ex24, para 328). The dosage forms included pulsatile release dosage forms that released PPI in two or more pulses separated by 0.5 to 4 hours, and that provided for targeted drug release in the small and/or large intestine. The extended release preparations comprised up to 500 mg of PPI, preferably between 5 and 100 mg, and most preferably between 10 and 80 mg. The application explained that with extended release, the plasma concentration of the PPI could

be kept at a high level for an extended time (Kahrilas, Ex31, para 208; Rowlings, Ex24, para 447).

[204] WO 093 taught an enteric coated PPI formulation that provided for discontinuous drug release of at least two consecutive pulses, separated by 0.5 to 12 hours (Rowlings, Ex24, para 335; Kahrilas, Ex31, para 224). The application exemplified its "best mode" as an enteric coated dual pulsed multiple release layered tablet where half the dose was in an immediate release core, coated using a semipermeable membrane that created a lag time while the second half was layered on top of the tablet and then covered with an enteric coat (Rowlings, Ex24, para 341). The dissolution profile demonstrated acid resistance, followed by two discrete pulses separated by 4 hours (Rowlings, Ex24, para 341). The dosage forms were said to improve therapeutic control of gastric acid secretion. The application stated that the dosage forms could comprise any PPI, in amounts of between 1 mg and 500 mg (TT 5A, 507:3-5, 509:16-19) and provided examples where the first and second dose amounts were the same (TT 5A, 569:19-23; TT4A, 451:12-24).

[205] WO 777 disclosed pulsatile release dosage forms of PPIs, including lansoprazole, designed to maintain gastric pH above 4 and deliver PPIs over a 24-hour period as a once daily administration for the treatment of GI disorders (WO 777, Ex32, Sch 6-31, 11:5-8; TT 5A, 512:26-513:1; Rowlings, Ex24, paras 343, 345; Davies, Ex32, para 541). The oral formulations were described as comprising first and second "populations" of solid dose units where the first population released quickly and the second population was formulated for delayed release (WO 777, Ex32, Sch 6-31, 9:17-36). The application explained that the amount of drug included in the

first and second populations of dose units may be different or identical (WO 777, Ex32, Sch 6-31, 10:30-31; TT 5A, 505:18-20; Davies, Ex32, para 380; Rowlings, Ex24, para 354; TT4A, 451:25-452:11), although no examples were provided where the second dose was higher than the first dose (TT 4A, 434:6-435:2; TT 5A, 572:19-573:10).

[206] Further, while one of the pulsatile release formulations in WO 777 had both pulses reaching a concentration of 100 ng/mL, the other formulation only had one of the two pulses reaching this plasma concentration. It was admitted by Dr. Rowlings that WO 777 did not teach 100 ng/mL as a threshold concentration for both pulses (TT 4A, 435:9-437:7).

[207] WO 584 described oral solution/suspension preparations of PPIs, including lansoprazole and its enantiomers, with a buffering agent that functioned to prevent or inhibit gastric acid degradation of the PPI in order to preserve its bioavailability and increase its absorption in the blood (Kahrilas, Ex31, paras 219-221; Davies, Ex32, para 385; TT4A, 456:26-457:12). In one example, the omeprazole preparation included both enteric coated PPI and non-enteric coated PPI, providing for two dose releases of 10 mg each, in different parts of the GI tract (WO 584, Ex32, Sch 6-33, 21:25-22:6; TT 4A, 438:26-439:15; Davies, Ex32, para 385; TT 8A, 1059:11-1060:6). The pharmaceutical compositions were said to be “particularly useful in patients who experience breakthrough gastritis between conventional doses, such as while sleeping or in the early morning hours” (WO 584, Ex32, Sch 6-33, 69:14-15; Davies, Ex32, para 386) and provided therapeutic effect over an interval up to about 24 hours after administration, allowing for once-a-day administration (WO 584, Ex32, Sch 6-33, 27:23-25). The application described formulations of the invention that yielded serum concentrations of PPI greater than about

0.1µg/mL (or 100 ng/mL) or 200 ng/mL, within 15 minutes after oral administration and from about 15 minutes to about 1.5 hours after administration (WO 584, Ex32, Sch 6-33, 18:21-19:12; Davies, Ex32, para 388; TT 5A, 506:12-21; Rowlings, Ex24, para 356), and claimed serum concentrations greater than 100 ng/mL. The compositions were described as being useful for both human and veterinary treatment, and provided examples of higher dose veterinary formulations for horses (WO 584, Ex32, Sch 6-33, 19:13-16, 29:22-24, 136:9-12; Davies, Ex32, para 387; TT 4A, 440:3-25).

[208] There were also a body of journal publications referenced by Dr. Davies and Dr. Kahrilas reporting on the pharmacokinetics of PPIs, one of which was a review article by Zimmermann, A.E., *et al*, "Lansoprazole: A Comprehensive Review", (1997), 17(2) Pharmacotherapy, 308-326 (Ex31, Sch 4-12) that summarized a number of the different PK studies on lansoprazole. Zimmermann reported C_{max} values for lansoprazole doses between 10 mg and 60 mg which ranged between 50 and 1771 ng/mL. Dr. Davies cites an even broader range of therapeutically relevant plasma concentrations for PPIs as a whole – 50 ng/mL to 2170 ng/mL (Davies, Ex32, para 411) – when the full scope of prior art journal publications are considered.

[209] There was no dispute from Takeda that the state of the art included knowledge of C_{max} values and plasma concentrations of PPIs that included the plasma concentrations set out in the Asserted Claims. While not expressly stated, the data from Puchalski, T.A, *et al*., "Pharmacodynamic Modeling of Lansoprazole Using an Indirect Irreversible Response Model", (2001), 412, Pharmacokin. Pharmacodyn., 251-258 (Ex32, Sch 6-38), when taken together, also suggested that at plasma concentrations of lansoprazole over 100 ng/mL a pH above a level of 4

was maintained for the majority of the day (Davies, Ex32, paras 424-429; TT 6A, 627:17-23 (with reference to WO 777 also), 629:5-26). Dr. Armstrong acknowledged that this would also hold true for dexlansoprazole (TT 8A, 1074:24-28). It was also known that there was a dose response and that as the dose of lansoprazole increased, there would also be a corresponding increase in gastric pH (TT 8A, 1033:7-13). However, the state of the art did not directly associate any particular plasma concentration as being required for therapeutic effect and did not study this relationship directly. It did not expressly identify any particular threshold plasma concentration as a target for therapeutic activity.

[210] In addition, as set out earlier, as a matter of CGK, the PSA knew that generally absorption of drugs occurred primarily in the small intestine and decreased farther down in the GI tract. Technology, such as the InteliSite® capsule, was available to study the absorption of a drug from various sites within the GI tract and had been used to study the absorption of the H_2 receptor antagonist, ranitidine, which was a compound also used to treat GI disorders (Rowlings, Ex24, para 97 and Pithavala, Sch 6-46; Davies, Ex32, paras 430-434 and Parr, Sch 7-9). However, the evidence was that these results were not directly translatable to other drugs. As acknowledged by Dr. Davies, the location where absorption is optimal would vary for every drug and every formulation (TT 6A, 670:6-20).

[211] As highlighted by Takeda, Dr. Rowlings, 5 years after the relevant date, felt that it was important to undertake a site-absorption study for drug development to understand the absorption of the drug in the GI tract (TT 4A, 463:26-464:25). He did not take for granted that the results for other drugs would be the same. It was not disputed by Apotex that no such studies had been

conducted on PPIs to investigate the extent of any differences in PPI absorption within the GI tract.

[212] While Apotex' experts asserted that it was a known dosing strategy to increase the dose of the drug to compensate for reduced absorption, they did not point to any prior art that taught this. Of the other pulsatile release drugs referenced as examples, there were some that used two equal doses and others like methylphenidate that used a higher second dose because of the known problem with tachyphylaxis requiring a higher second dose to overcome the problem of acute tolerance (TT 4A, 445:14-18). As was acknowledged by Dr. Rowlings, the design was guided by the drug's therapeutic goals (TT 4A, 448:18-449:2).

[213] Although there was a statement in WO 777 regarding having a second dose that could be higher than the first, there was no explanation as to why this would occur or any suggestion that this formulation would be preferred for absorption purposes. Indeed, the examples made by the inventors in WO 777 (as with WO 093 and WO 584) used equal amounts of PPI in each dose despite the second dose being absorbed at a later portion of the GI tract.

[214] Likewise, there was no suggestion from the 574 Application that the pulsatile PPI formulations should have a larger second dose to account for absorption differences. Rather, there were several formulations exemplified where the first and second doses were identical.

[215] I agree with Takeda, the state of the art did not expressly teach the PSA that regional absorption differences for PPIs should be addressed by making the second dose in a pulsatile dosage form greater than the first dose.

[216] Thus, it is my view that there were differences between the state of the art and the inventive concepts of the claims as of the relevant date.

(6) Do the Differences Constitute an Obvious Next Step?

[217] For the last step of the *Sanofi* analysis, I must consider whether there was a direct path to the inventive concept, including by experimentation. As such, the obvious to try test comes into play. As set out earlier, this involves consideration of whether it was more or less self-evident that any such experimentation ought to work; the extent, nature and amount of effort required to achieve the invention; and whether there was a motive provided in the prior art to find the solution the patent addresses.

[218] As noted above, the only evidence on the obvious to try analysis came from Apotex' experts. Dr. Armstrong did not conduct this analysis, nor did he consider the inventors' work (TT 8A, 1014:13-18).

[219] As stated by Dr. Kahrilas, nocturnal breakthrough was a known concern for patients suffering from GI disorders. While this problem was being managed in 2004 through the use of multiple dosing, the benefits of a once-a-day dosage form would have been apparent.

[220] Being aware of the issue of nocturnal breakthrough, both Dr. Rowlings and Dr. Davies gave evidence that the PSA would have been motivated to develop a once-daily dosage form that could deliver PPI at separate times to achieve prolonged acid suppression. While there were many types of dosage forms that could be chosen to achieve this objective, pulsed release dosage forms were one of the options that had specifically been taught and highlighted in the prior art through references such as the 574 Application, WO 777, WO 380 and WO 584, as providing advantages that included improved 24-hour acid suppression.

[221] The evidence indicated that once it was determined that the PK/PD relationship should be studied, the work of the inventors was straightforward and uneventful. Dr. Vakilynejad did not highlight any particular difficulties with the work conducted by the inventors, nor did he identify any surprises with the results obtained. Rather, his work adapted known models and techniques to available data (Davies, Ex32, paras 519, 533, 534, 536). However, there was no evidence supporting any motivation to target a threshold plasma concentration for the PPI as the starting point for the design of a dosage form or for the PSA to hone in on the plasma concentrations claimed as being threshold concentrations for pharmacological effect.

[222] There was no evidence that it would have been obvious to design a pulsatile dosage form based on the PPI's PK properties. The CGK was that although PPIs had a short half-life, they had a longer duration of effect; thus, there was believed to be no direct correlation between plasma concentration and therapeutic effect (TT 5A, 582:17-23). Even after the studies conducted for the 916 Patent, as expressly stated in Example 1, no direct relationship between gastric pH and PPI plasma concentration could be established (916 Patent, Ex1, 14:15-16).

[223] I agree with Takeda, without shifting the focus to the PPI's PK properties as the starting point for development there would be no basis to consider identifying a threshold concentration for therapeutic effect as the key to the formulation design. The fact that the plasma concentrations that are claimed are included within the range of disclosed C_{max} and plasma concentrations reported in the prior art tells the PSA nothing about their identification as a threshold plasma concentration for therapeutic effect.

[224] The second aspect of the inventive concept, in my view, follows from and is tied to the recognition of a threshold concentration. Without there being a focus on a threshold plasma concentration there would be no basis to consider absorption differences in the GI tract and to arrive at an increased second dose as part of the formulation design.

[225] As noted by Takeda, the state of the art was silent on the regional absorption of PPIs in the patient and its use as a dosing strategy for PPIs. Although there was a statement in WO 777 regarding having a second dose that could be higher than the first, there was no suggestion that this would be preferred for absorption purposes to achieve therapeutic effect and the examples all used equal amounts of PPI in each dose. There was only one reference (the 574 Application) that exemplified a higher second dose of PPI in a multi-dose formulation. However, this was one of many formulation options. There was no basis for the PSA to choose a dosage form with a second dose that was higher than the first dose over one where the first and second dose were equal. The 574 Application did not point to any particular dosage form design as being preferred over the other.

[226] Similarly, although Dr. Davies suggested that the PK/PD relationship had been studied in Puchalski and that this study suggested that at plasma concentrations of lansoprazole over 100 ng/mL, a pH level above 4 could be maintained for the majority of the day, none of the dose regimes administered to the patient group involved a higher second dose than the first dose. The concept of increasing the second dose to address GI absorption did not factor into the analysis.

[227] There was no direct path to the inventive concept and no basis for the PSA to embark on experimentation to arrive at the inventive concept without the need for inventiveness.

C. *Utility*

[228] To determine whether a patent discloses an invention with sufficient utility, the Court must first identify the subject-matter of the invention as claimed in the patent and second, ask whether that subject-matter is useful or capable of a practical purpose: *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36 [*AstraZeneca*] at para 54. A mere scintilla of utility is enough: *AstraZeneca* at para 55.

[229] The utility requirement in section 2 of the *Patent Act* is to be interpreted in line with its purpose; to prevent the patenting of fanciful, speculative or inoperative inventions: *AstraZeneca* at para 57.

[230] Utility can be either demonstrated or soundly predicted. To be soundly predicted, there must be a factual basis for the prediction; the inventor must have possessed an articulable line of reasoning from which the desired result could be inferred from the factual basis; and there must

be proper disclosure of the factual basis and line of reasoning in the patent: *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 [*Wellcome Foundation*] at para 70; *Eli Lilly Canada Inc v Novopharm Limited*, 2010 FCA 197 [*Eli Lilly*] at para 83. The patent may be sustained provided that a *prima facie* reasonable inference of utility exists: *Eli Lilly* at para 85.

[231] While there is no statutory requirement to disclose the utility of an invention (*Teva* at para 40; *AstraZeneca* at para 58), where the utility is founded on a sound prediction, the factual basis for the prediction must be set out in the patent disclosure to the extent it is not based on the CGK. As stated in *Bell Helicopter* at paragraph 153:

> [153] Where the factual basis can be found in scientifically accepted laws or principles or in information forming part of the common general knowledge of the skilled person, then no disclosure of such factual basis may be required in the specification. On the other hand, where the factual basis is reliant on data which does not form part of the common general knowledge, then disclosure in the specification may indeed be required to support a sound prediction.

(See also *Apotex Inc v Allergan Inc*, 2015 FCA 137 at paragraph 9):

> [9] The Federal Court identified the factual basis for the prediction (the minimum inhibitory concentration values of several compounds tested against a number of bacteria species together with comparative data) and the line of reasoning that would, to the skilled reader, flow from that data. As this Court observed in *Eurocopter v. Bell Helicopter Textron Canada Ltée*, 2013 FCA 219, 449 N.R. 111, at paragraphs 152 and 153, the factual basis, line of reasoning and level of disclosure required by the doctrine of sound prediction are to be assessed as a function of both the knowledge that the skilled person would have to base that prediction on and what the skilled person would understand as a logical line of reasoning leading to the utility of the invention. Those elements of the doctrine of sound prediction that would be self-evident to the skilled person need not be explicitly disclosed in the patent.

[232] The disclosure requirement was recently reiterated in *Pharmascience Inc v Teva Canada Innovation*, 2022 FCA 2 at paragraph 5:

> [5] Pharmascience argues that the Trial Judge erred with regard to the requirement for a proper disclosure by applying the disclosure requirement that is applicable to patents in general, and failing to recognize a heightened disclosure requirement applicable to inventions based on sound prediction. The doctrine of sound prediction calls for disclosure of the factual basis and line of reasoning..., unless such factual basis and line of reasoning would be self-evident to a person skilled in the art... This disclosure requirement exists because "the sound prediction is to some extent the *quid pro quo* the applicant offers in exchange for the patent monopoly": *Wellcome Foundation* at para 70.

[233] The parties agree that the practical utility of the Asserted Claims is the use of a dosage form with the claimed PK profile to give a pharmacological effect (*i.e.*, as agreed by the parties in this context, an effect on gastric acid pH). The outstanding issue is whether a sound prediction of that utility existed as of the filing date of the 916 Patent – that is, by June 1, 2005.

[234] There is no dispute that the only possible factual basis for the prediction that is disclosed in the 916 Patent is Examples 1 and 2 of the patent (Armstrong, Ex46, paras 167-168). However, Apotex asserts that Examples 1 and 2 are insufficient as there was a fatal assumption made in the patent relating to the results of the effect compartment modelling underlying Example 1, and there is a gap between what was modelled and what is claimed. As Example 1 is based on a PK/PD model, they rely heavily on the evidence of Dr. Davies, the only pharmacokinetics expert in the proceeding, to support these contentions. Indeed, Dr. Armstrong readily admitted that as a gastroenterologist he was not qualified to critically review the modelling work or Example 1 (TT 8A, 962:14-24).

[235] Apotex refers to Dr. Davies' testimony in which he asserts that a fatal assumption was made when equating the effect compartment concentrations to the steady state plasma concentrations in the patent (TT 6A, 613:20-615:8):

> A. Well, Example 1 is intravenous infusion data of lansoprazole, racemic lansoprazole. And it was modeled using PK-PD modeling, trying to model that relationship between plasma concentration and gastric pH, okay. That's what they did.
>
> And when they did that, they saw a characteristic anti-clockwise hysteresis loop. So there wasn't a direct relationship between concentration and effect, okay. So that is clear.
>
> Then – I think that is a good summation of Example 1.
>
> Then they went on further and modeled that to -- they took that, they knew that there wasn't a direct relationship, but they modeled it to a PK-PD model, where you have a central compartment. And I actually think they used a two compartment, where you have a central compartment, you have a tissue compartment. The drug moves from the central to tissues, but a small amount of it also moves to an effect compartment.
>
> And they modeled this data, and they came up with simulated effect concentrations in that small effect compartment, and they related that to simulated concentrations of pH. And they established Figure 1 based on that. So, really, on the X axis should be the simulated effect concentration in the effect compartment versus their effect data, which they also simulated. And they show here in this figure this relationship that we can see.
>
> Q. Professor Davies, you refer in the third bullet here to an assumption that was made. What would the skilled person understand with respect to that assumption?
>
> A. Well, the assumption is that the effect compartment concentrations are the same as your plasma concentrations. That's what they tell us. But the model shows clearly that they cannot be the same, because only a small amount of free drug can move to that effect compartment. And that's what -- you're modeling that to get these effect compartment concentrations.
>
> If they were the same, you wouldn't need to actually model it at all. You should just be able to relate the plasma concentrations to effect and get this relationship.

> They cannot be the same. So they made a fatal error in, in this assumption. They don't explain this assumption, but this cannot hold and does not hold. But that is what – and there's no explanation for, for doing that.

[236] Dr. Davies contends that the effect compartment concentrations would be lower than the plasma concentrations of the drug as it relates only to the free drug from the modelling. Thus, a direct correlation between the effect compartment concentration and steady state plasma concentration does not exist. As such, there is a disconnect between Example 1 and Figure 1 such that they cannot serve as a factual basis for the claims.

[237] Dr. Davies further asserts that there is a gap because the modelling in Example 1 is not based on data for an oral dosage form with two doses releasing as two pulses of PPI, but rather from the IV administration of lansoprazole. As such, he asserts that there is no consideration for any confounding food effects, circadian rhythm, and absorption; nor from oral dosing by a pulsed release dosage form (Davies, Ex32, para 574). He argues that there is no line of reasoning provided in the patent as to why a model that relates to a racemic lansoprazole infusion is predictive of the behaviour of orally administered dexlansoprazole released from a pulsatile release dosage form.

[238] Apotex seeks to parallel this case to *Eli Lilly Canada Inc v Apotex Inc*, 2009 FCA 97 [*Raloxifene*], in which the claim at issue covered the use of raloxifene in the treatment of osteoporosis in post-menopausal women. In *Raloxifene*, the patent disclosed a study on rats, but did not disclose the results of a study on 251 post-menopausal women suffering from osteoporosis (Hong Kong Study). At trial it was determined that the Hong Kong study was

necessary to turn the prediction contained in the claims of the patent into a sound prediction. This fact was not disputed on appeal. The FCA found that the failure to disclose the Hong Kong Study resulted in allegations of invalidity being found to be justified. As stated at paragraphs 12 and 15 of the decision:

> [12] ... the appellant at the hearing accepted for purposes of the appeal the conclusion reached by the Federal Court Judge at paragraphs 155 and 156 of his reasons that the Hong Kong study was required in order to turn the prediction on which the '356 Patent was predicated into a sound one. According to the Federal Court Judge, the Hong Kong abstract of the study conducted by the appellant on 251 post-menopausal women which concluded that "raloxifene show[ed] promise as a skeletal anti-resorptive" would have been a sufficient factual basis upon which a sound prediction of utility for raloxifene could have been made as of the filing date. However, this study was not disclosed in the '356 Patent with the result that the underlying factual basis for the prediction and the sound line of reasoning that grounded the inventors' prediction were not disclosed.
>
> [...]
>
> [15] In my respectful view, the Federal Court Judge proceeded on proper principle when he held, relying on *AZT*, that when a patent is based on a sound prediction, the disclosure must include the prediction. As the prediction was made sound by the Hong Kong study, this study had to be disclosed.

[239] In this case, Dr. Vakilynejad undertook modelling work to determine the relationship between plasma concentration and gastric pH. The work included modelling on the IV data from study M95-306 using a two compartment model with an effect compartment. However, Dr. Vakilynejad also conducted other modelling using the oral dosing data from M93-006 to create simulations that looked at the impact of dual-pulse dosing regimens on gastric pH, both for the whole day and for the nocturnal period (Vakilynejad, Ex2, paras 22-36, Modelling Report, Exhibit 2 to Vakilynejad Affidavit, Table 8, pages 13-15).

[240] Dr. Vakilynejad stated on cross-examination that the M93-006 modelling work was used to fit the model to the oral data (TT 1B, 38:17-39:13, 39:21-40:6):

> Q. Okay. So I want to – So I'm going to sort of put a little page break in here, if we can, between work that's in Example 1 of the 916 Patent, and moving toward to see what work you did after Example 1 of the 916 Patent.
>
> And continuing on page 12, moving into the work after – or, perhaps in the time after the patent – but moving to the work that's not included in Example 1 of the patent.
>
> A. Yes.
>
> Q. You now tell us that:
>
> "According to data obtained from study M93-006 and simulations performed using parameters estimates with equations 1, 2, 3, 4 and 6, the addition of second and/or third pulses over a 24 hour period clinically, significantly improved the overall pH control, particularly, at early evening and night." [As read]
>
> A. Okay.
>
> Q. So I just want to understand here, this is the M93-006 data again, so we're going back to the oral study now?
>
> A. Yes. ...
>
> [...]
>
> Q. And it was according to those data, the M93-006 data and simulations, that the addition of a second or a third pulse over 24 hours was shown to show significantly improved overall pH control, right?
>
> A. It shows, particularly, at the second part. Because sometimes when you look at the mean 24 hour, it might get diluted. But then, specifically, focusing on the later time, that's correct.
>
> Q. Okay. But my question here is more about what data went into that determination. It was the oral study data, the work that came after Example 1 of the 916 Patent?

> A. That is correct, oral data used to fit the model to oral data.

[241] As was explained by Dr. Vakilynejad, the data from the additional M93-006 modelling was used to "predict the effects of a variety of different dosage forms, such as those having two or three releases of drug at different time periods" (Vakilynejad, Ex2, para 34, Modelling Report, Exhibit 2 to Vakilynejad Affidavit, Table 8, pages 13-15). It was the additional modelling simulations involving the oral administration data from M93-006 that indicated to the inventors that as long as the drug was keep above the threshold concentration there would be an improvement in intragastric pH, and that a pulsatile release formulation could be used to achieve it (TT 1B, 46:25-47:25).

[242] As acknowledged by Dr. Vakilynejad, the M93-006 study and the modelling simulations of the effect of pulsatile release formulations of lansoprazole on gastric pH were not referenced in the 916 Patent (TT 1B, 47:26-48:15). The description in Example 1 was limited to discussion of the modelling based on M95-306 and its IV lansoprazole data (TT 1B, 38:8-16; 916 Patent, Ex1, 14:12-15:2).

[243] In his report Dr. Davies explained that an IV infusion of lansoprazole is a different input than an oral dosage form and would be expected to give a different output. He asserts that one cannot serve as the basis for predicting a PD response by the other (Davies, Ex32, para 580, see also TT 6A 637:17-27):

> ...even assuming that the modelling of Example 1 is appropriate for determining the plasma concentration of intravenous lansoprazole that will result in a desired pharmacodynamic effect, which it is not, this model relates only to a racemic lansoprazole infusion

> formulation, and not oral formulations of PPIs generally (as included in claims 1, 5 to 11), or dexlansoprazole specifically (as included in claim 16). As seen in the Internal Takeda Documents, differences in the input rates for intravenous and oral administration and the models selected for each route of administration, which information is not disclosed in the 916 Patent, impact the expected pharmacodynamic response (*e.g.*, the effect on intragastric pH....). The 916 Patent provides no line of reasoning whatsoever as to why this model is also predictive of the behaviour of other PPIs administered orally.

[244] Apotex asserts that until the oral data simulations were conducted, the effect of a pulsatile release dosage form on gastric pH could not have been predicted.

[245] As highlighted by Takeda, the factual basis does not need to be confirmatory, but only sufficient to allow a *prima facie* reasonable inference of utility: *Eli Lilly* at para 85. Sound prediction presupposes that further work is required: *Eli Lilly* at para 82. The level of disclosure is to be assessed as a function of the knowledge the PSA would have to base the prediction on, and as a function of what the PSA would understand as a logical line of reasoning leading to the utility of the invention: *Bell Helicopter* para 152.

[246] Takeda argues that there is no utility issue as both Dr. Davies and Dr. Kahrilas acknowledged that there would be a pharmacological effect (*i.e.*, an effect on gastric acid pH) from an oral dosage form made in accordance with the Asserted Claims (TT 7A, 795:22-796:6; TT 5A, 579:5-14). Takeda asserts that utility is therefore a matter of CGK and there is no need to rely on Example 1. Rather, Example 1 relates to subsection 27(3) of the *Patent Act* and disclosure of the invention – *i.e.*, the threshold concentration.

[247] Further, even if Example 1 were necessary to serve as the factual basis for the prediction, Takeda argues that the modelling work described in Example 1 is sufficient to support a reasonable inference that there would be a pharmacological effect from the claimed dosage form. Takeda distinguishes the mere scintilla of practical utility that is required from what was necessary for the inventors to investigate the effect of the dosage form on nocturnal breakthrough. They alleged that no expert established that the threshold concentration of 100 ng/mL was erroneous. As such, they assert that Dr. Davies' criticisms of Example 1 do not amount to an arguable defence under this ground, and are inconsistent with positions given for his obviousness analysis.

[248] However, the problem I have with Takeda's argument is that it is not supported by the balance of the evidence and the rules of evidence.

[249] As highlighted by Apotex, after-the-fact confirmations as to utility by the PSA cannot satisfy the prediction as of the filing date (*Wellcome Foundation* at para 84). While Dr. Davies and Dr. Kahrilas stated that if a dosage form were made in accordance with claim 1, they would expect such dosage form to provide a pharmacological effect, that response was not qualified as to time. The evidence says nothing about what was known at the filing date. There is no assertion that pulsatile release dosage forms of PPIs were part of the CGK. Nor is there any suggestion in the 916 Patent that prior art studies on PPIs served as the foundation for any prediction of utility.

[250] It is clear from the evidence of Dr. Vakilynejad, including his Modelling Report, that it was only after the additional modelling and simulation work with the M93-006 oral data that he

made PK and PD parameter predictions or estimates for lansoprazole pulsatile formulations, including estimates covering the 24 hour period. I agree with Apotex, the evidence supports the view that until the oral data simulations were conducted, the effect of the pulsatile release dosage form claimed on gastric pH could not be predicted.

[251] Without this data in the 916 Patent, the PSA would not have the line of reasoning used by the inventors to predict that the dosage form proposed would achieve the practical utility and would not be able to fill that gap with their CGK.

[252] Further, there is no contrary expert evidence to rebut the comments made by Dr. Davies as to the difficulties with Example 1. I agree with Apotex that any attempted reliance by Takeda on evidence given by Dr. Davies for his obviousness opinions as an attempt to undermine his comments regarding Example 1 are improper as any such perceived inconsistencies were not put to Dr. Davies in cross-examination, thereby allowing him an opportunity to explain the alleged contradictions: *Browne v Dunn* (1893), 1893 CanLII 65 (FOREP), 6 R. 67 (HL (Eng)).

[253] In my view, the 916 Patent does not provide proper disclosure of the factual basis and line of reasoning to support a sound prediction of utility and the Asserted Claims are invalid for this reason. The lack of sufficient disclosure is further reflected in my subsection 27(3) analysis below.

D. *Insufficiency*

[254] Pursuant to subsections 27(3)(a) and (b) of the *Patent Act*:

Specification	**Mémoire descriptif**
(3) The specification of an invention must	**(3)** 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;

[255] The specification, which includes the claims and the disclosure, must define the “precise and exact extent” of the privilege being claimed so that 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 their application: *Teva* at para 70.

[256] The PSA must be able to produce the invention using only the instructions contained within the disclosure and the PSA's CGK: *Teva* at paras 50, 71; *Teva Canada Ltd v Leo Pharma Inc*, 2017 FCA 50 [*Leo Pharma*] at paras 43-44.

[257] The disclosure must teach the PSA how to put the invention into practice, without the need for exercising inventive ingenuity or undue experimentation. A disclosure is insufficient if it necessitates the working out of a problem: *Idenix Pharmaceuticals Inc v Gilead Pharmasset LLC*, 2017 FCA 161 at para 19. While a minor research project is too much, some non-inventive trial and error experimentation may be permitted: *Seedlings Life Science Ventures, LLC v Pfizer Canada ULC*, 2021 FCA 154 [*Seedlings*] at para 68; *Leo Pharma* at para 59; *Teva* at para 75.

[258] In this case, the deficiencies with the disclosure of the 916 Patent are two-fold. First, Example 1 does not provide sufficient information for the PSA to understand how the inventors arrived at the oral dosage data and steady state plasma concentrations in the patent. As highlighted earlier and explained by Dr. Davies, the experimentation said to underlie Example 1 yielded modelled results that would be known to the PSA to be significantly lower than actual steady state plasma concentration values. Further, the data was from an IV study alone at one time point and did not include the subsequent oral dosage modelling data that was necessary for the inventors to translate the results of the modelling to threshold concentrations for a pulsatile release oral dosage form to be used over a 24 hour time period.

[259] Even taking Figure 1 on its face, the PSA would read the model as predicting that at a steady state plasma concentration of 100 ng/mL a patient will have a mean pH of about 2.4 (TT

8A, 1101:22-27), which is a more acidic pH than what is required to successfully treat GI disorders such as GERD (TT 8A, 1069:2-7). It is the same pH that the model would predict for plasma concentrations of between 25 and 75 ng/mL (TT 8A, 1101:28-1102:4). To reach a mean pH of 4, a patient would need a plasma concentration of about 300 ng/mL (TT 8A, 1102:10-13).

[260] While Takeda argues that this is a disguised attack under section 53 of the *Patent Act*, in my view it falls squarely as a question of sufficiency and whether the PSA would be able to understand the invention, how the threshold concentrations were chosen, and what they represent. A proper understanding of Example 1 and the data from Figure 1 is essential for the PSA to be able to make the same successful use of the invention as the inventor could at the time of their application.

[261] Second, the Asserted Claims are directed to a dosage form that achieves a particular pharmacokinetic threshold plasma concentration through pulsatile release of drug. However, there is no teaching or example in the 916 Patent of any particular dosage form that would satisfy the Asserted Claims.

[262] The 916 Patent leaves open the possibility that any dosage form that delivers a PPI at the specified threshold level, regardless of the type of formulation technology used to achieve the pharmacokinetics, could be encompassed within the scope of the invention (Rowlings, Ex24, para 476). However, it is undisputed that the PSA would have to work through potential options for formulating a dosage form and conduct experimentation, including administration of the

dosage form to a human patient, and measuring their plasma concentration at different points of time, in order to determine if the parameters of the Asserted Claims are met.

[263] Both Dr. Rowlings and Dr. Davies described the work required to achieve the desired dosage form as a minor research project that would involve working through potential options disclosed in the patent literature as to formulation technology, appropriate polymers, coatings, and candidate dosage forms, followed by evaluation of the pharmacokinetics of the dosage form and administration in a human to measure the plasma concentration after each dose is released (Rowlings, Ex24, paras 478-480; Davies Ex32, paras 637-638). There would also need to be adjustments to determine dose amounts.

[264] Dr. Timko similarly acknowledged that a significant number of steps would be required to arrive at the invention, including formulation work, administration of the dosage form to a human, bioavailability and bioequivalence studies, followed by dose adjustments, but described this work as trial and error research (Timko, Ex11, paras 22-33; TT 2A, 215:6-218:16).

[265] However, Dr. Timko viewed routine work broadly and as permissibly including a research project, short of what would be a eureka moment (TT 2B, 149:1-20).

[266] He admitted that the 916 Patent did not provide guidance and could not, for example, point to any literature reference that could assist with determining the dose amounts (TT 2A, 213:28-215:5).

[267] In *Teva*, the missing disclosure that gave rise to the insufficient disclosure finding was the identification of which of two compounds had been demonstrated to be useful in the treatment of erectile dysfunction. The work required to fill in the missing information comprised administering the compounds to humans and monitoring the pharmacological response of such experimentation. While this experimentation was routine and non-inventive work, it nonetheless required a minor research project and was found to require too much of the PSA to render the disclosure sufficient.

> [73] Although Patent '446 includes the statement that "one of the especially preferred compounds induces penile erection in impotent males", the specification does not indicate that sildenafil is the effective compound, that Claim 7 contains the compound that works, or that the remaining compounds in the patent had been found not to be effective in treating ED"...The claims were structured as "cascading claims", with Claim 1 involving over 260 quintillion compounds, Claims 2 to 5 concerning progressively smaller groups of compounds, and Claims 6 and 7 each relating to an individual compound.
>
> [74] The disclosure in the specification would not have enabled the public "to make the same successful use of the invention as the inventor could at the time of his application", because even if a skilled reader could have narrowed the effective compound down to the ones in Claim 6 and Claim 7, further testing would have been required to determine which of those two compounds was actually effective in treating ED. As the trial judge stated, ... "[a] skilled reader would then conduct tests on those two compounds and determine which of those compounds worked". ... "the skilled reader must undertake a minor research project to determine which claim is the true invention".
>
> [75] Pfizer argued in the Court of Appeal that Teva had already been able to make the same use of the invention having only the specification, because it had filed a submission with the Minister of Health for a drug product containing sildenafil ... However, this does not change the fact that the specification required, at a minimum, "a minor research project" in order to determine whether Claim 6 or Claim 7 contained the correct compound. The fact that Teva carried out this minor research project is irrelevant to Pfizer's obligation to fully disclose the invention. ...

[268] While here the missing information does not involve determining which of two compounds are useful, it nonetheless involves putting the subject-matter of the claim into practice. The work required to fill in the missing information and arrive at the claimed dosage form involves at least as much work as that set out in *Teva*. This gap is much more than what is contemplated by the *Patent Act*. The disclosure given in the 916 Patent is, in my view, insufficient to support the invention of the 916 Patent.

E. *Claims Broader*

[269] The claims of a patent will be overbroad where a feature is missing from the claims that is so essential to the invention that its absence undesirably changes the scope of the invention such that it encompasses embodiments that were not contemplated by the disclosure or by the inventors: *Seedlings* at para 54.

[270] In final argument, Apotex' overbreadth argument narrowed to one argument: that the claims were overbroad because the work of the inventors established that at least 1 hour was required between the pulsed doses; however, this 1 hour was not claimed.

[271] However, I do not agree that this argument is borne out by the evidence or the Court's construction of the Asserted Claims. First, the modelling report on which Apotex relies does not state that there *must* be any particular time gap between pulses, but only that certain time gaps were studied, with some being more desirable than others (Modelling Report, Ex2, Exhibit 2 to Vakilynejad Affidavit, page 16):

> The addition of second pulse 1 to 20 h after the first pulse of the drug resulted in a significant improvement in the control of

> intragastric pH. However, the most desirable and optimum pH control occurred when the second pulse was introduced 6 to 12 h after the first pulse.

[272] Moreover, the Asserted Claims refer to the first dose and the second dose being released from the dosage form as "discrete pulses of the PPI". As set out earlier, it is the Court's view that the term "discrete" as used in the Asserted Claims would be understood by the PSA as indicating that there is some noticeable time period between the pulses on a plasma concentration-time profile.

[273] Apotex relies heavily on the testimony of Dr. Timko who interpreted the claims as being without a limit as to time or delay between the release of the first and second pulses. In a series of questions on cross-examination relating to this view of the claims and the inventors' work, Dr. Timko agreed to the following propositions (TT 1B, 166:10-16):

> Q. So what we saw was that the inventors' work related to a delay of between one and 20, correct?
>
> A. Correct.
>
> Q. And the claims are broader in the sense that they allow for an inclusion of formulations in which there is no limit?
>
> A. Right.

[274] However, the reference to breadth in Dr. Timko's answer must be taken with caution. Dr. Timko is not a lawyer and has not, in my view, adopted this expression with the same legal significance Apotex seeks to impose. Whether the Asserted Claims are overly broad is a matter for the Court alone to determine. The use of such soundbites from a witness falls short of satisfying me that the legal test has been met.

F. *Ambiguity*

[275] Section 27(4) of the *Patent Act* requires that the patent specification end with a claim or claims that define distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed.

[276] As set out in *Western Oilfield Equipment Rentals Ltd v M-I LLC*, 2021 FCA 24 at paragraph 121: “The basis for invalidity due to ambiguity is that the patent must give adequate notice to the public as to what activities are claimed as exclusive to the patentee. If a skilled person is able to construe the claims, that notice is provided.”

[277] In this case, there can be no dispute that the claims are capable of being construed as set out above. While there may be a dispute as to what the construction should be, a dispute over the meaning to be given to certain terms does not render the claims ambiguous.

[278] Apotex’ argument as to ambiguity relies on the Court adopting a construction of the claims that is entirely functional, which it has not done. The fact that there is some functional language in the claim does not render the claims meaningless or incapable of discernment, especially where the functional property is clearly understood and is determinable: *Burton Parsons Chemicals Inc v Hewlett-Packard (Canada) Ltd*, [1972] FCJ No 1126 at para 23, 7 CPR (2d) 198; *Schering-Plough Canada Inc v Pharmascience Inc*, 2009 FC 1128 at paras 60 and 213; *Generics [UK] Limited (t/a Mylan) v Yeda Research and Development Co Ltd et al*, [2013] EWCA Civ 925 (EWCA) at para 78.

[279] The attack on the validity of the Asserted Claims on the basis of ambiguity is without merit.

G. *Unpatentable Subject-matter*

[280] A patent claims valid subject-matter where the claims are directed to subject-matter that is capable of physical existence, is a vendible product, or is something that manifests a discernible effect or change: *Amazon.com Inc v Canada (Attorney General)*, 2011 FCA 328 at para 66.

[281] Apotex argues that the Asserted Claims seek to monopolize any pulsed release dosage form that achieves the claimed pharmacokinetic result, without regard to how the pharmacokinetic result is achieved. As such, they argue that the Asserted Claims are directed to a desired result, and not to a novel dosage form. I cannot agree.

[282] While the Asserted Claims are "formulation-agnostic" in the sense that they are not limited, for example, to pulsed dosage forms that require two discrete populations of granules or beads within the dosage form, this does not, in my view, equate to the claims being directed to a desired result.

[283] The Asserted Claims are directed to a physical dosage form (*i.e.*, a vendible product) that must be loaded with a first and a second dose of PPI, each of which must have 5 to 300 mg of PPI, with the second dose containing at least 10% more PPI than the first dose, depending on the

claim. As acknowledged by the experts, the dosage form releases PPI in a manner that would provide a practical effect (*i.e.*, an effect on gastric acid pH).

[284] The Asserted Claims are not directed to unpatentable subject-matter.

IX. Conclusion

[285] Thus, while I find that Apotex has not met its burden with respect to certain of the invalidity grounds alleged, it is my view that it has established that Takeda did not meet its obligation to set out the factual basis and line of reasoning for its prediction of utility relating to the subject-matter of the Asserted Claims. Further, the 916 Patent fails to correctly and fully describe the invention and its operation or use as contemplated by the inventors, contrary to subsection of 27(3) of the *Patent Act.*

[286] Taken together with my earlier finding, it is my view that the Asserted Claims of the 916 Patent are both not infringed and invalid and that the action should be dismissed.

X. Costs

[287] The parties provided brief oral submissions on costs at the close of trial, each agreeing that costs should be awarded to the successful party based on a lump sum of actual legal fees. Takeda asserted that the appropriate rate in this case should be 25% of legal fees, along with 100% of reasonably incurred disbursements.

[288] Apotex relied on the decision of Chief Justice Crampton *in Allergan Inc v Sandoz Canada Inc*, 2021 FC 186 [*Sandoz*] which established that in proceedings under the *PMNOC Regulations*, the starting point for lump sum costs should be at the mid-point between 25-50% percent; that is at 37.5% (at paragraph 34). Apotex argued that an appropriate award of costs for this case should be 50% of the successful party's legal fees along with reasonable disbursements. They also asserted that Takeda should be required to pay a lump sum amount representing 100% of legal fees and disbursements relating to those steps involving the 369 Patent as this was not ultimately pursued at trial. Apotex highlights that the allegations relating to the 369 Patent were abandoned on the eve of the delivery of expert reports resulting in additional, unnecessary costs being incurred.

[289] Takeda takes issue with this latter point, highlighting that while a request for formulation details relating to Apotex' samples was made on July 21, 2022, the requested samples were only provided on April 19, 2023. Upon receipt of the information, it asserts that its experts immediately conducted their analysis with Apotex being advised that the allegations relating to the 369 Patent were being dropped on May 24, 2023. Takeda contends that there is no authority for 100% recovery of legal fees under these circumstances. I agree. On the facts presented, there is no basis to treat the costs associated with the 369 Patent any different from those relating to the 916 Patent.

[290] While I agree that a lump sum award of 37.5% should be taken as the starting point as set out in *Sandoz*, this does not take me to the 50% requested by Apotex. In my view, a cost award that is 40% of Apotex' legal fees and 100% of reasonable disbursements is more appropriate in

the circumstances. This award reflects Apotex' success on both non-infringement and invalidity, while acknowledging that there were certain invalidity grounds on which they were not successful, some of which need not have been pursued and served to add to the complexity of the proceeding unnecessarily.

[291] In particular, it is noted that Apotex pursued eight grounds of invalidity through to trial and only dropped one before argument. Even then, while it dropped its Gillette Defence prior to argument, it needlessly pursued a pleadings motion relating to this ground in the days before trial, unnecessarily diverting the parties' and the Court's attention to an issue that did not form part of its trial evidence and it did not pursue. In light of all of this, it is my view that a 40% lump sum award, along with reasonable disbursements is reasonable.

JUDGMENT IN T-151-22

THIS COURT'S JUDGMENT is that:

1. The action is dismissed.

2. Costs are awarded to Apotex on a lump sum basis set at 40% of its legal fees, along with 100% of its reasonably incurred disbursements. This same rate applies to the costs awarded for the steps relating to the 369 Patent. Should the parties be unable to agree on the specific amount of costs to be paid they may make further submissions of no more than seven (7) pages each to the Court, with Apotex serving and filing their submissions within thirty (30) days of the date of this Judgment, followed by Takeda serving and filing its submissions thirty (30) days thereafter. Apotex shall be permitted to serve and file a brief reply of no more than three pages within fifteen (15) days of receiving Takeda's responding submissions.

"Angela Furlanetto"
Judge

FEDERAL COURT

SOLICITORS OF RECORD

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