Federal Court Cour fédérale

Date: 20210112

Dockets: T-97-19
T-98-19
T-503-19
T-504-19

Citation: 2021 FC 1

Ottawa, Ontario, January 12, 2021

PRESENT: The Honourable Mr. Justice Zinn

Docket: T-97-19

BETWEEN:

BRISTOL-MYERS SQUIBB CANADA CO. AND BRISTOL-MYERS SQUIBB HOLDINGS IRELAND UNLIMITED COMPANY

Plaintiffs

and

PHARMASCIENCE INC.

Defendant

Docket: T-98-19

AND BETWEEN:

BRISTOL-MYERS SQUIBB CANADA CO. AND BRISTOL-MYERS SQUIBB HOLDINGS IRELAND UNLIMITED COMPANY, AND PFIZER INC.

Plaintiffs

and

PHARMASCIENCE INC.

Defendant

Docket: T-503-19

AND BETWEEN:

BRISTOL-MYERS SQUIBB CANADA CO. AND BRISTOL-MYERS SQUIBB HOLDINGS IRELAND UNLIMITED COMPANY, AND PFIZER INC.

Plaintiffs

and

SANDOZ CANADA INC.

Defendant

Docket: T-504-19

AND BETWEEN:

BRISTOL-MYERS SQUIBB CANADA CO. AND BRISTOL-MYERS SQUIBB HOLDINGS IRELAND UNLIMITED COMPANY

Plaintiffs

and

SANDOZ CANADA INC.

Defendant

AMENDED PUBLIC JUDGMENT AND REASONS

(The Confidential Judgment and Reasons were issued on January 4, 2021, amended pursuant to Rule 397(2) on January 8, 2021, and no redactions are necessary)

[1] On consent, these four actions were tried "on a coordinated basis." The Plaintiffs [collectively referred to as BMS] commenced these actions pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 to prevent the Defendants, Pharmascience Inc. [Pharmascience] and Sandoz Canada Inc. [Sandoz] from obtaining notices of compliance to market their generic versions of BMS's product ELIQUIS™.

[2] ELIQUIS is an anticoagulant that blocks certain clotting proteins in the blood; specifically, it is a Factor Xa [FXa] inhibitor. Two patents relating to ELIQUIS are at issue. Canadian Patent No. 2,461,202 [the 202 Patent] relates to apixaban, the active pharmaceutical ingredient in ELIQUIS. It is at issue in Court Files T-97-19 and T-504-19. Canadian Patent No. 2,791,171 [the 171 Patent] relates to the formulation of the BMS 2.5 and 5 mg apixaban tablets. It is at issue in Court Files T-98-19 and T-503-19.

BRIEF BACKGROUND

[3] The factual evidence of Dr. Donald J. P. Pinto and Dr. Jantin Patel as to the history of the research and development of ELIQUIS by BMS, and its predecessors, is largely undisputed. Numerous pharmaceutical companies were doing research to find a compound to replace Warfarin, which was then the standard pharmaceutical used to treat and prevent blood clots. Warfarin was a difficult drug therapy to administer, for at least two reasons: It had dangerous side effects and put the patient at risk of heavy bleeding, and it required that patients constantly

undergo testing. These factors were the impetus to find a replacement therapy that was more easily administered.

[4] Initial research by BMS in the early 1990s focused on drugs that would inhibit the enzyme thrombin. In 1996, its focus shifted to compounds that would inhibit the enzyme FXa.

[5] Dr. Pinto attests that in 2001, BMS "finally discovered apixaban: a structurally differentiated, potent, safe, and selective Factor Xa inhibitor with a unique and special set of pharmacokinetic properties." The 202 Patent, which claims apixaban, was filed in Canada on September 17, 2002. It has a publication date of April 3, 2003, and was issued on July 12, 2011.

[6] The 171 Patent deals with the tablet formulation of apixaban. The development team was formed in 2001 and it took some 7 years to develop the now patented formulation for ELIQUIS. The 171 Patent was filed February 2, 2011. It has a publication date of September 1, 2011, and issued on August 29, 2017.

JOINT STATEMENT OF ISSUES

[7] The parties very helpfully prepared and submitted to the Court for its benefit, a Joint Statement of Issues, which is reproduced below:

> 1. The asserted claims in these actions are as follows ("**Asserted Claims**"):
>
> a. **202 Patent** (Court File Nos. T-97-19, T-504-19):

i. Claim 2; Claim 4 as it depends on claim 2; and Claims 5 to 7, as each depends on claim 4, as it depends on claim 2.

b. **171 Patent** (Court File No. T-98-19):

i. Claim 18 as it depends on claim 14, as it depends on either claim 13 or 12, as either depends on claim 6, as it depends on claim 5, as it depends on claim 4; and

ii. Claims 30-32, as each depends on claim 29, as it depends on claim 25, as it depends on claim 24, as it depends on claim 23.

c. **171 Patent** (Court File No. T-503-19):

i. Claim 18 as it depends on claim 14, as it depends on either claim 13 or 12, as either depends on claim 6, as it depends on claim 5, as it depends on claim 4; and

ii. Claims 30-31, as each depends on claim 29, as it depends on claim 25, as it depends on claim 24, as it depends on claim 23.

2. The Defendants have confirmed that their only non-infringement allegation is that none of the Asserted Claims will be infringed because they are invalid. Furthermore, the Defendants agree that should the Court find any of the Asserted Claims to be valid, then the orders sought by the Plaintiffs in these actions shall issue. In other words, there will be no trial on infringement issues other than with respect to the validity of the Asserted Claims, and the parties agree that the Plaintiffs are not required to establish any infringement of the essential elements of any asserted patent claim for the purposes of these actions.

3. Without prejudice to the Plaintiffs' arguments about validity and the way in which the below validity allegations have been legally framed by the Defendants, the Defendants intend to raise the following validity allegations.

A. The '202 Patent – Court File Nos. T-97-19 and T-504-19

4. The issue to be determined in Court File Nos. T-97-19 (BMS v. Pharmascience) and T-504-19 (BMS v. Sandoz) is whether any of the asserted claims of the '202 Patent is valid and thus would be

infringed, and more specifically, the validity issues that Pharmascience and Sandoz presently intend to raise are:

(i) **Insufficiency** – Does the '202 Patent satisfy the requirements of subsections 27(3)(a) and (b) of the *Patent Act*?

(ii) **Double Patenting** – Are the asserted claims of the '202 Patent invalid for double patenting in light of Canadian Patent No. 2,349,330 ("the '330 Patent")?

(iii) **Anticipation** – Is the subject matter defined by the asserted claims of the '202 Patent anticipated by the '330 Patent (or its equivalent international patent application, i.e. WO 00/39131)?

(iv) **Obviousness** – As of the claim date (September 21, 2001), would the subject matter defined by the asserted claims of the '202 Patent have been obvious to a person skilled in the art?

(v) **Overbreadth** – Are the asserted claims of the '202 Patent overbroad for claiming more than what the inventors made or disclosed?

(vi**) Inutility** – Are the asserted claims of the '202 Patent invalid for lack of utility, i.e. no demonstration or sound prediction of utility?

(vii) **Insufficiency and Inutility of a Selection Patent** – Is apixaban one of the compounds covered by the '330 Patent? If so, are the asserted claims of the '202 Patent invalid for failing to disclose a substantial advantage over the compounds covered by the '330 Patent, or are the asserted claims of the '202 Patent invalid because the claimed compound has no substantial advantage over the compounds covered by the '330 Patent?

B. The '171 Patent – Court File Nos. T-98-19 (Pharmascience) and T-503-19 (Sandoz):

5. The issue to be determined in Court File Nos. T-98-19 (BMS v. Pharmascience) and T-503-19 (BMS v. Sandoz) is whether any of the asserted claims of Canadian Patent No. 2,791,171 ("the '171 Patent") is valid and thus would be infringed, and more

> specifically, the validity issues that Pharmascience and Sandoz presently intend to raise are:
>
> > (i) **Obviousness** – As of the claim date (February 25, 2010), would the subject matter defined by the asserted claims of the '171 Patent have been obvious to a person skilled in the art?
> >
> > (ii) **Overbreadth** – Are the asserted claims of the '171 Patent overbroad for claiming more than what the inventors made or disclosed?
> >
> > (iii) **Insufficiency** – Does the '171 Patent satisfy the requirements of subsections 27(3)(a) and (b) of the *Patent Act*?
> >
> > (iv) **Inutility** – Are the asserted claims of the '171 Patent invalid for lack of utility, i.e. no demonstration or sound prediction of utility?
> >
> > (v) **Ambiguity** – Does the '171 Patent satisfy the requirements of subsection 27(4) of the *Patent Act*?

[8] As noted, the only non-infringement allegation raised by the Defendants is that none of the asserted claims identified above [the Asserted Claims] in these two patents will be infringed because they are invalid. Pursuant to subsection 43(2) of the *Patent Act*, RSC, 1985, c P-4, the 202 Patent, and the 171 Patent are presumed to be valid. The burden of proving invalidity rests with the Defendants.

EXPERT WITNESSES

[9] A number of expert witnesses were called by the parties. Based on the record before the Court, their agreement on qualifications was accepted:

A. Expert witnesses called by Pharmascience

Dr. Michael Rieder is an expert physician and clinical pharmacologist with expertise in in vitro and in vivo pharmacologic research and clinical trials.

Dr. Paul Laskar is an expert in pharmaceutical formulation and drug delivery, including with respect to pre-formulation assessment, formulation design and development, manufacture, characterization, testing and analysis, including for solid oral dosage forms.

B. Expert witnesses called by Sandoz

Dr. Eliot Ohlstein is an expert pharmacologist, with expertise in drug discovery and development, and with a particular focus in the area of cardiovascular biology.

Dr. Michael Chong is an expert organic chemist, with expertise in organic chemistry and synthetic organic chemistry.

Dr. John Gleason is an expert in medicinal chemistry, with expertise in drug discovery and development.

Dr. Gordon Moe is an expert cardiologist, with expertise in the treatment and prevention of thromboembolic diseases.

Dr. Arthur Kibbe is an expert in pharmaceutical formulation and drug delivery, including with respect to pre-formulation assessment, formulation design and development, manufacture, characterization, testing and analysis, including for solid oral dosage forms.

C. Expert witnesses called by BMS

Dr. Jeffrey Weitz is an expert hematologist, with expertise in the treatment and research of thrombosis, the coagulation cascade, as well as, pre-clinical and clinical trials relating to anticoagulants.

Dr. David Taft is an expert pharmacokineticist.

Dr. Martyn Davies is an expert in pharmaceutical formulation and drug delivery, including with respect to pre-formulation assessment, formulation design and development, manufacture, characterization, testing and analysis, including for solid oral dosage forms.

[10] The Defendants submit that their experts ought to be preferred over those called by BMS.

[11] With respect to Dr. Weitz, they note that (1) he has a "close relationship" with BMS that he wants to continue, (2) he "heaped praise on apixaban" while failing to disclose that it was in fact the entire class of direct oral anti-coagulants [DOACs] that shifted practice, and (3) he was evasive, rejecting a principle from his own paper "that the DOACs 'which include dabigatran, rivaroxaban, apixaban and edoxaban' have 'similar efficacy, better safety and greater convenience'" than Warfarin, which he accepted only after the paper was put to him.

[12] I do not accept the Defendants' submission regarding the weight to be given to Dr. Weitz's evidence.

[13] Dr. Weitz readily acknowledged his relationship with BMS, and testified that he had done work with many pharmaceutical companies. He executed the Rule 52.2 Code of Conduct for Expert Witnesses, and gave the Court no reason to think that he failed to observe it.

[14] Dr. Weitz does state that apixaban is unique among DOACs. He attests that while he has prescribed all the DOACs approved in Canada, ELIQUIS is his preferred choice for patients at high risk of bleeding. He notes that the *New England Journal of Medicine* in 2019 recognized ELIQUIS as a practice-changing drug. He further attests that in his "own experiences with ELIQUIS reflect what a practice-changing drug it has been." Respectfully, while DOACs may have collectively changed practice, it is clear to the Court, from this witness's evidence and that of others, that ELIQUIS is the most significant of them.

[15] Dr. Weitz's evidence when asked on cross-examination if the DOACs "have similar efficacy, better safety, and greater convenience than drugs such as Warfarin" was:

> No, I wouldn't conclude that. … I think that there are differences amongst these agents in how they performed against Warfarin, and to say that one is better than another, well, you would have to have head-to-head trials. But they did show differences as in the trials, and we use that information as clinicians to select one versus the other when treating our patients.

[16] In his paper put to him in cross-examination, he wrote:

> The direct oral anticoagulants, DOACs, which include dabigatran, rivaroxaban, apixaban and edoxaban, can be given in fixed doses without routine coagulation monitoring. In clinical trials the DOACs have been shown to be at least as effective as vitamin K antagonists such as Warfarin for stroke prevention in non-valvular atrial fibrillation and for treatment of venous thromboembolism and to produce less serious bleeding. With similar efficacy, better safety, and greater convenience, the DOACs are now replacing VKAs for these indications."

[17] He accepted that as accurate when he wrote it, and when asked if that was not inconsistent with his oral evidence, stated:

> When I made that statement I'm looking, if you put all the data together with all the DOACs compared with Warfarin, that is the conclusion you come up with. But again, each DOAC compared with Warfarin, some different results in each of these trials. As a class, yes, what I'm saying here is accurate.

[18] I find that Dr. Weitz was not evasive in his evidence, nor inconsistent. As a class of drugs, he accepted that the DOACs were superior to Warfarin, but noted that each, when compared with Warfarin, gave different results such that one cannot say that one is better than the others without a head-to-head trial.

[19] With respect to Dr. Taft, the Defendants submit, "he was woefully inexperienced compared to the Defendants' experts when it came to the key issue of FXa inhibitors." However, his evidence was not directed to FXa inhibitors:

> Counsel asked for my opinion about what, if anything, the skilled person or team would understand the 202 Patent to teach or disclose about the objects of the invention and subject-matter of the claims of the 202 Patent, when read in light of their common general knowledge as of its publication date (April 3, 2003).

[20] He was also asked to review the prior art relied upon by the Defendants (Canadian Patent No. 2,349, 330 [the 330 Patent] and Patent Application WO 00/39131), from the perspective of the skilled person and offer his opinion whether either rendered obvious the 202 Patent. An in-depth knowledge of FXa inhibitors is not required for that purpose.

[21] The Defendants also submit that his reading of the 202 Patent was "skewed" as "he ignored the clear language of the patent, or read-in concepts that are totally absent, whenever it served the position of BMS." I reject the suggestion that he tailored his evidence to support the position of BMS. He offered his opinion and there is no evidence, in my view, that it was not arrived at honestly. At the end of the day, the question of the proper interpretation, which we shall come to shorty, is that of the trial judge and not that of any witness.

[22] The Defendants lastly submit that this witness was evasive and they point to his rejection of a principle from his own earlier writings. The relevant portion of the cross-examination follows:

> Q. Would you also agree that knowledge of protein binding is necessary to determine the suitable dosage for <u>initial testing</u> in humans? [emphasis added]

> A. Again, I don't believe the initial testing in humans would require consideration of protein binding. Initial testing in humans are phase 1 studies, and phase 1 studies are done at low doses, at least at the beginning, to establish safety and evaluate pharmacokinetics. And so no, I don't necessarily think protein binding would be a critical determination of that dose. [emphasis added]
>
> …
>
> Q. [The article] starts:
>
> "Nevertheless protein binding measurements are important during drug development for several reasons first, interspecies differences will effect allometric predictions of PK parameters. Second, knowledge of drug protein binding is necessary for establishing a suitable dose in humans."
>
> And is that an accurate statement?
>
> A. I have no reason to discount that statement, no. I think if you look at the beginning of the paragraph it's referring to Dr. Bennett's publication and the discussion of whether protein binding is important for drug-drug interactions. But I have no reason to dispute that statement, no.

[23] I find that the statement in the article about a "suitable dose" in humans is directed to the same issue as the question posed about the dosage in the initial testing in humans. There is no "rejection" as alleged. In any event, I do not find that Dr. Taft was evasive in his testimony.

[24] I did find that Dr. Laskar, an expert called by the Defendants, was often unresponsive in cross-examination. Rather than answer the question asked, he often responded with an answer to a different question. He had to be reminded that he was called as a witness to assist the Court (and not the party paying him), and that responses that failed to address the questions asked were unhelpful. For this reason, whenever his testimony varied from another, I prefer the evidence of the other witness.

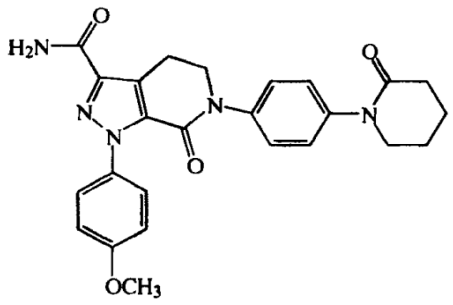
PERSON OF SKILL IN THE ART

[25] A patent is to be read purposively, through the eyes of a skilled person, with a mind willing to understand: *Whirlpool Corp v Camco Inc*, 2000 SCC 67 [*Whirlpool*] and *Free World Trust v Electro Santé Inc*, 2000 SCC 66 [*Free World Trust*]. There is no material dispute between the parties as to the person of skill in the art. As regards the 202 Patent, the skilled person is a team comprising a medicinal chemist, a pharmacologist or pharmacokineticist, and a clinician. As regards the 171 Patent, the skilled person is a skilled formulator.

[26] The Court's first task is to construe the claims in light of the patent specification as a whole to ascertain the scope of the invention as claimed.

THE 202 PATENT

[27] The claims of the 202 Patent in issue are Claims 2 and 4 to 7, which read as follows:

> 2. A compound represented by the following formula:
>
> 
>
>
> 4. Use of a compound of claim 1 or 2 in the treatment of a thromboembolic disorder.
>
> 5. Use according to claim 4 wherein the thromboembolic disorder is ischemic sudden death, transient ischemic attack or stroke.

> 6. Use according to claim 4 wherein the thromboembolic disorder is deep vein thrombosis.
>
> 7. Use according to claim 4 wherein the thromboembolic disorder is pulmonary embolism.

[28] Apixaban is the compound represented in Claim 2.

[29] The Defendants submit that BMS called no evidence on the interpretation of the claims of the 202 Patent and thus their experts' opinions that is reproduced below is all that is before the Court:

> The opinions of Drs. Ohlstein and Rieder indicate the claims should be construed as follows:
>
> • **Claim 2:** The composition of matter, now known as apixaban, assumed to be used to treat or prevent thromboembolic disorders in humans and non-human mammals.
>
> • **Claim 4:** Use of apixaban, to treat or prevent thromboembolic disorders, in humans and non-human mammals, with the exception of conditions that are only treated in humans (i.e. acute coronary syndrome, ischemic sudden death, transient ischemic attacks, and deep vein thrombosis).
>
> • **Claim 5-7:** The same as claim 4, but where the thromboembolic disorder is as follows: Claim 5 – ischemic sudden death, transient ischemic attack or stroke; Claim 6 – deep vein thrombosis; and Claim 7 – pulmonary embolism.
>
> [emphasis added]

[30] I agree with BMS that the "Defendants' attempt to read into the claims of the 202 Patent that the invention must treat both humans and non-human mammals is contrary to the 202 Patent's clear teaching that treatment is directed to 'mammals' – and any mammal will do." The

term “treatment” is defined in the disclosure of the 202 Patent as being treatment of a disease in a mammal:

> As used herein, "treating" or "treatment" cover the treatment of a disease-state in a mammal, particularly in a human, and include: (a) preventing the disease-state from occurring in a mammal, in particular, when such mammal is predisposed to the disease-state but has not yet been diagnosed as having it; (b) inhibiting the disease-state, i.e., arresting it development; and/or (c) relieving the disease-state, i.e., causing regression of the disease state. [emphasis added]

[31] If apixaban worked only in non-human mammals, it would still fall within the 202 Patent.

[32] In my view, the proper construction of the Asserted Claims in the 202 Patent is two-fold. Claim 2 of the 202 Patent is a claim to the chemical known as apixaban. Claims 4 to 7 claim the use of apixaban in a mammal in the treatment or prevention of thromboembolic disorders, including ischemic sudden death, transient ischemic attack or stroke (Claim 5), deep vein thrombosis (Claim 6), and pulmonary embolism (Claim 7).

Insufficiency of Disclosure

[33] Subsection 27(2) of the *Patent Act* provides that an application for a patent must contain a petition and a specification of the invention. The specification is comprised of the disclosure and the claims. If all the requirements for the issuance of a patent under that *Patent Act* are met, then, as required by subsection 27(1) of the Act, the Commissioner of Patents “shall grant a patent for an invention.”

[34] Subsections 27(3) and (4) of the *Patent Act* set out the requirements for a proper disclosure:

(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;
(c) in the case of a machine, explain the principle of the machine and the best mode in which the inventor has contemplated the application of that principle; and	c) s'il s'agit d'une machine, en expliquer clairement le principe et la meilleure manière dont son inventeur en a conçu l'application;
(d) in the case of a process, explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions.	d) s'il s'agit d'un procédé, expliquer la suite nécessaire, le cas échéant, des diverses phases du procédé, de façon à distinguer l'invention en cause d'autres inventions.
(4) The specification must end with a claim or claims defining distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed.	**(4)** Le mémoire descriptif se termine par une ou plusieurs revendications définissant distinctement et en des termes explicites l'objet de l'invention

dont le demandeur revendique la propriété ou le privilège exclusif.

[35] In *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60, [*Sildenafil SCC*] at paras 69-71, the Supreme Court of Canada, pointing to its earlier judgment in *Consolboard Inc v MacMillan Bloedel (Saskatchewan) Limited*, [1981] SCR 504, makes it clear that for there to be sufficiency of disclosure, "the specification, which includes the claims and the disclosure, must define the 'precise and exact extent' of the privilege being claimed so as to ensure that the public can, *having only the specification*, make the same use of the invention as the inventor [italics in original]." There are three questions to be asked: (1) What is your invention?, (2) How does it work?, and (3) Does the description enable a person skilled in the art or the field of the invention to produce it using only the instructions contained in the disclosure? If the public cannot do that, then the disclosure is insufficient, and the patent invalid.

[36] The Defendants note that in *Sildenafil SCC*, the Supreme Court at paragraph 90 observed, "the relevant question is whether the disclosure was sufficient as of the date of filing [emphasis added]."

[37] Dr. Chong testified that the application for the 202 Patent, as filed and published (that is, the patent application), claimed 10^{100} compounds. It was only just before the 202 Patent issued that BMS narrowed the claims to one compound - apixaban. The Defendants submit that prior to narrowing the claim, the disclosure was insufficient because as of the date of publication one could not make the invention.

[38] BMS agrees that this Court has held in *Novartis Pharmaceuticals Canada Inc v Teva Canada Limited*, 2013 FC 283 [*Zoledronate FC*]; aff'd 2013 FCA 244, that sufficiency of the disclosure is to be assessed as of the date of publication. However, BMS submits that the Defendants confuse the date of assessment with the document to be assessed as of that date.

[39] The Defendants write that *Zoledronate FC* was the first comprehensive review of the issue since the Supreme Court's decision in *Sildenafil SCC*:

> Hughes J. determined that the date of publication was the most appropriate date as this was "the date that the public is seized with the application", and also the date the patentee "has committed to claims for the invention in a manner available to the public". Thus, Hughes J. considered the content of the patent as published, not the content of the patent as filed. [emphasis added]

[40] There is a passage in *Zoledronate FC* that appears to support the Defendants' submission as to the document to be assessed for sufficiency as of the date of publication. Justice Hughes notes at paragraph 178 that the patent he was considering, when originally filed as an application, contained claims to many compounds, including zoledronate, but the issued patent claimed only zoledronate. He states:

> If I were to consider sufficiency as of the date of filing the application, I would find that the application was no different than that considered by the Supreme Court in *Teva*, and thus invalid for lack of sufficient disclosure. [emphasis added]

[41] The Supreme Court of Canada in *Sildenafil SCC* did not consider the application, but the issued patent. I do not accept that *Zoledronate FC* stands for the proposition urged on this Court by the Defendants. The question that is always before the Court is whether the patent is valid or

whether or not an Asserted Claim is valid or not. It is not whether some document that pre-existed it is valid or whether some subsequently abandoned "claim" is invalid or not.

[42] The Defendants submit, at paragraph 32 of their written submissions, that the "date of publication was the date used to assess sufficiency of disclosure in other Federal Court cases." They reference *Alcon Canada Inc v Cobalt Pharmaceuticals Co*, 2014 FC 149 at para 236, and *Hospira Healthcare v Kennedy Trust for Rheumatology*, 2018 FC 259 at paras 6 and 246, aff'd on this ground 2020 FCA 30 at paras 101-104.

[43] I agree that in each of those decisions the Court stated that sufficiency was to be determined as of the date of publication; however, none indicates that the document examined for sufficiency was that available on that date, rather then the patent as issued.

[44] The Defendants further submit that "the date of filing has also been relied on in several cases, and according to the FCA, 'anything which occurred subsequent thereto is of no relevance':" *Novopharm Limited v Pfizer Canada*, 2010 FCA 242 [*Sildenafil FCA*], at para 79. They also reference *Cobalt Pharmaceuticals v Bayer Inc*, 2015 FCA 116, para 67, and *Eli Lilly Canada v Apotex*, 2018 FC 736, para 123.

[45] The passage in paragraph 79 of *Sildenafil FCA* that the Defendants quote is the following:

> As to the appellant's arguments regarding certain of the Judge's comments, which the appellant labels "extraneous", I have no difficulty agreeing with the Pfizer that these comments do not lead to a reviewable error. Pfizer correctly points out that the Judge

> was required to determine whether the disclosure was sufficient as of the date of filing. As a result, anything, which occurred subsequent thereto, is of no relevance. Nevertheless, in my view, the Judge's comments, although misguided in the circumstances, do not form the basis of a reviewable error. As the relevant invention is the compound found in Claim 7, the disclosure is sufficient.

[46] The "extraneous" comments are described at paragraph 46, and are these:

> Second, the appellant asserts that the Judge took into account irrelevant and extraneous factors, specifically that the appellant waited 13 years to challenge the validity of the patent (until 2007), that Pfizer identified sildenafil as the active ingredient 11 years ago and that Viagra was introduced in the United States nine years ago.

[47] With this context, the statement that anything that occurred subsequent to the date of filing is irrelevant does not support the Defendants' submission. All that is being noted is that the Judge's comments related to facts occurring after the filing date and they are irrelevant to whether as of the filing date, the disclosure was sufficient. The Federal Court of Appeal examined the patent as issued, something that occurred subsequent to filing.

[48] I agree with BMS's submission that this Court's role is to examine sufficiency of the issued claims for the reasons BMS offers:

> [T]he *Patent Act* expressly contemplates and permits post-filing changes to the specification, including changes as occurred in this case. It is not the role of the Court to reassess what occurred during prosecution. <u>It is for the Commissioner of Patents to determine whether a patent application is sufficient. It is for the court to determine whether the granted patent is sufficient.</u> [emphasis added]
>
> …

> Were it otherwise, it would lead to the absurd result that the post-filing procedures contemplated by the Patent Act (e.g. claim amendments, divisional amendments, reissuance, disclaimer) would be rendered moot for sufficiency but not for other grounds of invalidity.

[49] The test for sufficiency is whether, applying the knowledge of the person skilled in the art at the relevant time (date of publication), he or she is in a position to work the invention. The invention is that claimed in the patent, and until it is issued, there is no patent.

[50] The Defendants submit that wording of the 202 Patent as issued, fails for insufficiency for four reasons. First, it does not teach that apixaban is potent or selective. Second, it is silent on apixaban's risk of causing excessive bleeding. Third, it is silent on apixaban's pharmacokinetic profile. Fourth, it included dosing information in relation to humans that BMS knew to be wrong.

[51] Throughout the trial, the Defendants asked witnesses "Where's the data?" meaning where is the data in the patent that supports that apixaban is useful in treating thromboembolic disorders. The question relates to the first three of the reasons the Defendants advance in support of their insufficiency submission.

[52] The Federal Court of Appeal in *Pfizer Canada Inc v Canada (Health)*, 2008 FCA 108 [*Lipitor FCA*] makes it clear that whether there is data in the patent that substantiates the invention is irrelevant:

> The Applications Judge was wrong in interpreting the disclosure requirement of subsection 27(3) of the Act as requiring that a patentee back up his invention by data. By so doing, he confused

> the requirements that an invention be new, useful and non-obvious with the requirement under subsection 27(3) that the specification disclose the "use" to which the inventor conceived the invention could be put: see *Consolboard, supra*, at 527. Whether or not a patentee has obtained enough data to substantiate its invention is, in my view, an irrelevant consideration with respect to the application of subsection 27(3). An analysis thereunder is concerned with the sufficiency of the disclosure, not the sufficiency of the data underlying the invention. Allowing Ranbaxy to attack the utility, novelty and/or obviousness of the 546 patent through the disclosure requirement unduly broadens the scope of an inventor's obligation under subsection 27(3) and disregards the purpose of this provision. [emphasis added]

[53] I accept the evidence of Dr. Weitz in cross-examination, that by singling out apixaban in the claims, the patent tells the skilled person that the inventors had determined apixaban to be a safe, potent and selective FXa inhibitor with antithrombotic efficacy:

> Q. So a skilled person looking at a pharmaceutical patent wouldn't assume that the compound worked, because they would also know that the majority of them don't work, isn't that fair?
>
> A. Right, but when you go from this huge genus down to one compound, I think the skilled person would think it's extremely unlikely that they're going to put forward a compound that didn't work and to claim that amongst this huge genus, because then you're putting your eggs in one basket here. You've gotta have -- the thinking has got to be that this is a compound that has the desired characteristics and is the one that you're going to take forward.
>
> …
>
> So no, I think that the skilled person would take this and say these people must have found a compound that has the properties they're looking for, that's why they're claiming this particular compound out of this huge genus for a treatment of thromboembolic disorders. Of course I would like to see the data, but just because I'm not seeing it doesn't mean the data don't exist, and it doesn't mean that they haven't done it.

[54] The fourth reason submitted by the Defendants for the patent's insufficiency of disclosure is that the 202 Patent provided false dosing information in relation to humans. That information is found at page 182 of the 202 Patent:

> By way of general guidance, the daily oral dosage of each active ingredient, when used for the indicated effects, will range between about 0.001 to 1000 mg/kg of body weight, preferably between about 0.01 to 100 mg/kg of body weight per day, and most preferably between about 1.0 to 20 mg/kg/day.

[55] This passage is not directed specifically to humans. Indeed, it is preceded by the statement, "A physician or veterinarian can determine and prescribe the effective amount of the drug required to prevent, counter, or arrest the progress of the thromboembolic disorder" [emphasis added].

[56] The Defendants' expert, Dr. Ohlstein, in cross-examination agreed that the skilled person would read this as being only general guidance:

> Q. And so a person of skill in the art reading this would understand that it's really for the physician or veterinarian to determine the right or correct dose, right?
>
> A. Agreed.
>
> Q. Right. And just like your patent, the skilled physician would be expected to be able to determine the correct dose, yes?
>
> A. Yes.
>
> Q. And they could do that as part of their routine skill and judgment, yes?
>
> A. Yes.
>
> Q. And what follows then by way of general guidance is just that general guidance, correct?
>
> A. Yes.

> Q. And when it gives the dosage ranges below from point 1 to 1000 milligrams, they're not recommending a particular dose for apixaban there, are they?
>
> A. No.
>
> Q. And when they give the preferred range, not recommending a dose for apixaban are they?
>
> A. No.
>
> Q. And when they give the most preferred range they're not recommending a dose for apixaban?
>
> A. Okay, no.

[57] I find that the impugned passage, being only general guidance, cannot be said to be providing false dosing information.

[58] For these reasons, I reject the submission that the 202 Patent is invalid for insufficiency of disclosure.

Inutility

[59] Section 2 of the *Patent Act* provides that an invention must be "new and useful." Utility must have been demonstrated or soundly predicted as of the filing date: *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36, paras 49, 54–57 and *Sildenafil SCC*, para 40.

[60] The Defendants submit that "[i]n cases of demonstrated utility, the reference to the study demonstrating utility ***must*** be contained within the patent disclosure so that the public will know that utility has been demonstrated even though the actual evidence or proof of demonstrated

utility need not be set out in the patent disclosure" [emphasis in original]. They cite and rely on *Apotex Inc v Pfizer Canada Inc*, 2011 FCA 236, at para 30 which follows *Sildenafil FCA* at para 90:

> The appellant's argument that Pfizer was required to include evidence of demonstrated utility in the patent disclosure is without merit. The requirements for demonstrated utility can be provided in evidence during invalidity proceedings as opposed to in the patent itself. So long as the disclosure makes reference to a study demonstrating utility, there do not appear to be any other requirements to fulfil section 2. [emphasis added]

[61] This statement by the Federal Court of Appeal has been expressly rejected by the Supreme Court of Canada in *Sildenafil SCC* at paras 39-40:

> That the invention must be useful as of the date of the claim or as of the time of filing is consistent with this Court's comments in AZT, at para. 56:
>
> > Where the new use is the *gravamen* of the invention, the utility required for patentability (s. 2) must, as of the priority date, either be demonstrated or be a sound prediction based on the information and expertise then available. If a patent sought to be supported on the basis of sound prediction is subsequently challenged, the challenge will succeed if . . . the prediction at the date of application was not sound, or, irrespective of the soundness of the prediction, "[t]here is evidence of lack of utility in respect of some of the area covered". [Italics in original; underlining added.]
>
> Nothing in this passage suggests that utility is a disclosure requirement; all it says is that "the utility required for patentability (s. 2) must, as of the priority date, either be demonstrated or be a sound prediction". Utility can be demonstrated by, for example, conducting tests, but this does not mean that there is a separate requirement for the disclosure of utility. In fact, there is no requirement whatsoever in s. 27(3) to disclose the utility of the invention: see, e.g., *Consolboard*, at p. 521, per Dickson J.: "I am further of the opinion that s. 36(1) [now s. 27(3)] does not impose

> upon a patentee the obligation of establishing the utility of the invention". [emphasis added]

[62] More recently, and to the same effect, is the Supreme Court of Canada's statement at para 58 of *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36 [*Esomeprazole SCC*]:

> Even though utility of the subject-matter is a requirement of patent validity, a patentee is not required to disclose the utility of the invention to fulfill the requirements of s. 2. As was stated by Dickson J. in *Consolboard*:
>
> > ... I do not read the concluding words of s. 36(1) [now s. 27(4)] as obligating the inventor in his disclosure or claims to describe in what respect the invention is new or in what way it is useful. He must say what it is he claims to have invented. [p. 526]
>
> See also *Teva*, at para 40.

[63] The Defendants further submit that utility had not been demonstrated as of the filing date as apixaban had been tested in healthy animals but "had not yet been administered to humans, nor had any human clinical studies commenced."

[64] The Supreme Court of Canada at paras 54-55 of *Esomeprazole SCC* set out the approach to be followed in analyzing utility and the nature of the usefulness required to be demonstrated or soundly predicted:

> To determine whether a patent discloses an invention with sufficient utility under s. 2, courts should undertake the following analysis. First, courts must identify the subject-matter of the invention as claimed in the patent. Second, courts must ask whether that subject-matter is useful — is it capable of a practical purpose (i.e. an actual result)?

> The Act does not prescribe the degree or quantum of usefulness required, or that every potential use be realized — a scintilla of utility will do. A single use related to the nature of the subject-matter is sufficient ….

[65] The subject matter of the 202 Patent is two-fold: it is the compound apixaban (Claim 2) and the use of apixaban in treating thromboembolic disorders in mammals (Claims 4-7).

[66] BMS observes that "[e]stablishing that a compound has the ability to inhibit a target implicated in a disease is doubtlessly a useful discovery" citing *Bristol-Myers Squibb Canada Co v Apotex Inc*, 2017 FCA 190 at para 40. I accept the evidence of Dr. Weitz and Dr. Pinto that the *in vitro* testing demonstrated that apixaban selectively and potently inhibited FXa, a key target implicated in the treatment of thrombosis, and possessed the desired pharmacokinetic profile of low volume of distribution and ultra-low clearance. The utility of Claim 2 was therefore demonstrated as of the filing date.

[67] The subject matter of Claims 4-7 is using apixaban in treating thromboembolic disorders in mammals. The evidence is that studies and tests completed prior to the filing date, showed:

> Apixaban is a potent and selective inhibitor of coagulation factor Xa. As such, it produces anticoagulant effects in vitro and in vivo. In models of thrombosis in rabbits, rats and dogs, apixaban demonstrated anti-thrombotic efficacy at doses which resulted in modest changes in standard coagulation assays.

[68] Moreover, as BMS notes in its written submissions, the Defendants' experts agreed that these studies and tests showed that apixaban was effective in treating thromboembolic disorders in the animals tested:

> Dr. Rieder acknowledged the preclinical studies comprised "solid data" which shows "not only does the drug inhibit Xa, it also reduces thrombus formation". According to Dr. Rieder "it is no question that in these animals, these rats, rabbits and dogs, apixaban is anti-thrombotic." Dr. Ohlstein agreed that "BMS did a fairly comprehensive pre-clinical workup of apixaban, and had a good understanding of its pharmacological, pharmacokinetic, drug metabolism and safety profile." [emphasis in original]

[69] I do not accept the Defendants' submission that these test animals were healthy and thus the tests proved nothing regarding treatment. These were not "healthy animals" at the time they were tested. Clot formation in the otherwise healthy animals was induced, thereby causing thrombosis and rendering them unhealthy prior to administering the test treatment.

[70] I find that prior to the filing date BMS had demonstrated the effectiveness of apixaban in treating thromboembolic disorders in mammals. Although BMS is not required to demonstrate effectiveness in humans, in cross-examination, Dr. Weitz testified that the studies "demonstrated that it worked in mammals, in rats, rabbits and dogs and that information … as I said, it very strongly suggests and really leaves no doubt that it's going to do the same in humans" [emphasis added].

[71] I therefore find that BMS had demonstrated the utility of the 202 Patent as at the filing date.

Prior Art – The 330 Patent

[72] The Defendants assert that the 330 Patent filed by BMS prior to the 220 Patent (or its equivalent international patent application, WO 00/39131, [collectively referred to as the 330 Patent]), is prior art that invalidates the 220 Patent on grounds of anticipation, obviousness, and double patenting.

[73] An invention is not "new" as required by section 2 of the *Patent Act*, if the same thing has been done before, publicly. It is not new because it has been anticipated. Section 28.3 of the *Patent Act* stipulates that the subject matter defined by a claim must be something that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains. Lastly, double patenting is impermissible. One cannot obtain a patent where a prior patent has been issued to the same person for the same invention, based on the theory that doing so would breach the initial bargain for a monopoly for the invention for a specified limited period.

Anticipation

[74] There are two inquiries to be made when assessing anticipation: disclosure and enablement: *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 [*Sanofi*] at paras 25-27. In order to be found to be anticipatory, the single piece of prior art (the 303 Patent), must both (1) disclose the invention of the patent at issue (the 202 Patent), and (2) enable the skilled person to make the invention using that prior art and common knowledge, allowing for some trial and error experimentation to make it work.

[75] The Supreme Court of Canada in *Free World Trust* at para 26 approved the test for anticipation described in *Beloit Canada Ltd. v. Valmet OY* (1986), 8 C.P.R. (3d) 289 (FCA) [*Beloit*], at p. 297, and noted that the test was difficult to meet:

> One must, in effect, be able to look at a prior, single publication and find in it all the information which, for practical purposes, is needed to produce the claimed invention without the exercise of any inventive skill. The prior publication must contain so clear a direction that a skilled person reading and following it would in every case and without possibility of error be led to the claimed invention.

[76] In *Lipitor FCA* at para 83, Justice Nadon, citing *Sanofi* and other authorities, found that anticipation had not been proven in that case. The first patent was a genus patent and the second a selection patent:

> The allegation of anticipation, in my view, is not justified. A claim to a specific chemical compound cannot be anticipated by a prior art reference which only teaches a broad class of genus of compounds into which the compound falls because the prior art reference does not give directions which inevitably result in the specific compound (see *Sanofi-Synthelabo Canada Inc. v. Apotex Inc.* (2005), 39 C.P.R. (4th) 202 (F.C.) at paragraph 55, affirmed 2006 FCA 421 (F.C.A.) at paragraphs 25-27; *Pfizer Canada Inc. v. Apotex Inc.*, [1997] F.C.J. No. 1087, 77 C.P.R. (3d) 547 (Fed. T.D.); *Pfizer Canada Inc. v. Canada (Minister of Health)*, 2006 FCA 214, [2006] F.C.J. No. 894 (F.C.A.)). [emphasis added]

I find the evidence here parallels that in *Lipitor FCA*.

[77] In its reply to the Defendants' request to admit, BMS stated, "Apixaban falls within the scope of at least one claim of the Canadian Patent No. 2,349,330 (the "'330 Patent")." Dr. Chong testified that apixaban is covered by claims 1, 2, 3, 4, 8 and 9 of the 330 Patent.

[78] The 330 Patent describes its field of invention to be:

> This invention relates generally to nitrogen containing heterobicycles, which are inhibitors of trypsin-like serine protease enzymes, especially factor Xa, pharmaceutical compositions containing the same, and methods of using the same as anticoagulant agents for treatment and prevention of thromboembolic disorders.

[79] It is a genus patent, i.e. it discloses a large genus or class of possible compounds useful in the treatment and prevention of thromboembolic disorders. Both Dr. Weitz and Dr. Gleason testified that the skilled person reading the 330 Patent would understand that not all of the claimed compounds would be useful in treating and preventing thromboembolic disorders; rather they were compounds that had the "potential" to do so.

[80] Dr. Chong in cross-examination volunteered that he had done a mathematical calculation of the number of compounds disclosed in the 330 Patent. His response reveals the immense number of compounds covered by that patent:

> Q. Claim 1 depicts 66 distinct cores, correct?
>
> A. I didn't count them. Yeah, I'll just take your word for it now, yes.
>
> Q. And they're distinct scaffolds because the orientation of the substituents could differ, some rings are bigger, some have different substituents. They're all distinct, correct, each of these scaffolds?
>
> A. Yes. As you say, they have different sizes and substituents that are in place. They're all similar in the assumption of heterobicyclic system.
>
> Q. As you point out in your calculation, even though claim 1 depicts 66 of these cores, and I'll just scan them through quickly, there is actually variability even amongst the scaffolds, such that

you approximated there are actually 78 different scaffolds, I think you call them generic skeletons, is that right?

A. Yes.

Q. So let's turn up those skeletons that you depict, Dr. Chong. I'm going to zoom out so we can all look at it together. What you did was you looked at the 78 different scaffolds and you categorized them into four types, correct?

A. That's right.

Q. There's type 1A, there's type 1B, type 2A, type 2B, and each of these types contain various number of scaffolds?

A. That's right.

Q. I would like to consider the type 1A scaffold with you just so we can understand what it represents. So number one, this category of scaffold you identify as there being 27 distinct scaffolds within this category, correct?

A. Yes.

Q. And within the scaffold, as you pointed out earlier, there's various substituents, and for each substituent, you did the effort to calculate the number of possibilities at each of the substituents on the scaffold, correct?

A. That's right.

Q. If we look at type 1A, if we look at the B position alone which is one position on the scaffold, that position has two times 10 to the 65 possibilities, correct?

A. That was an estimate I did, yes.

Q. It's actually higher.

A. I don't -- I don't doubt you for a minute.

Q. And that two times 10 to the 65, just so we can put some context to it, a trillion as I understand it is 10 to the power of 12, right?

A. When I did these and saw these big numbers, I think I actually looked for some comparisons in some way of trying to think of these things, and I think I looked for the number of stars in

the universe, and that was on the order of maybe 10 to the 25th. So still a much smaller number than the numbers that you see -- that we all see in front of us now. [emphasis added]

Q. So the B position, to use your comparison, has more stars than the universe?

A. Yes.

Q. And same for the A position, more possibilities than stars in the universe?

A. Yes.

Q. Same for the Z position, more stars than in the universe?

A. Yes.

Q. And same for the G position?

A. If that number that I tried to remember, 25th, is correct, then yes.

Q. So when you add those up, those permutations, that's why it's astronomical. Maybe stars in the universe is the appropriate metaphor for astronomical. That's how you get to 10 to the 28, when you account for all those permutations, right?

A. I basically just did the arithmetic.

Q. And that arithmetic, when you add up all the possibilities for that type of scaffold, approximately 10 to the 227, correct?

A. Some number that is just larger than I can think about.

Q. When you say that apixaban is covered by claim 1 of the 330 Patent, what you're saying is that it's one compound within this large number that you can't think about? More stars than the universe?

A. I'm saying that if I look at the different substituents that are in place and I do the substitutions, then apixaban is one of the compounds.

Q. And it's one of the compounds in claim 1 which I think you just said is a number larger than you can think about, correct?

A. It's a very large number.

Q. It's a number bigger than you can think about, those were your words?

A. Than I want to think about, yes.

Q. You also reviewed, for the purpose of seeing whether apixaban falls within them, claims 2 to 6 as well, right?

A. Yes.

Q. Those claims also cover a variety of cores, a variety of substituents, those also covered an astronomically high number of combinations?

A. They would be very large numbers.

Q. Each of those claims also cover in excess of 10 to the 100 number of compounds?

A. Whatever number you want to put on it, it is a very large number.

Q. Just so it's clear for the record, can we put 10 to the 100 on each of those, at least?

A. Actually when I did these calculations, I did it for the ones that were listed in the one claim, and I don't doubt that the other ones are large. How restrictive they are compared to claim 1, I don't really know.

Q. You would agree with me, though, at least it's more stars in the universe to use your number of 10 to the 25?

A. It would be a very large number, yes.

Q. Larger than 10 to the 25?

A. I would expect so.

[81] Given the enormous number of compounds in the 330 Patent that could potentially be useful in treating and preventing thromboembolic disorders, it is hardly surprising that Dr. Gleason, the Defendants' expert, in cross-examination testified that finding apixaban would require more than trial and error:

Q. Right. And how many of those would be useful to treat thromboembolic disorders, given your testimony that we have many more failures than successes in trying to figure that out?

A. I could not put a percentage on it.

Q. It would be a small percentage?

A. That would have all of the properties that it takes to be a drug that would have all of the developability characteristics?

Q. One that would be safe and effective to treat thromboembolic disorders?

A. It would be a relatively small percentage.

Q. And you'd agree with me that -- sorry. It would be a small percentage?

A. It would be a small percentage.

Q. And you'd agree with me that it would be a research project to figure out which ones are useful to treat thromboembolic disorders?

A. Of those -- of the compounds that were not made? Yes.

Q. The person of skill in the art would basically have to do what BMS did to find apixaban?

A. Yes.

[82] Moreover, Dr. Gleason testified that the 330 Patent did not provide any instruction on how to make apixaban:

Q. Just while we're at the 330 Patent, can you agree with me that apixaban is not specifically claimed in the 330 Patent?

A. Yes, I agree. It's not.

Q. The structure of apixaban is not depicted anywhere in the 330 Patent?

A. It is not.

> Q. The chemical name for apixaban is not set out anywhere in the 330 Patent?
>
> A. It is not.
>
> Q. None of the examples in the 330 Patent describes how to make apixaban?
>
> A. That's correct.

[83] On the record before the Court, I am unable to conclude that a person skilled in the art and reading the 330 Patent would be able to identify apixaban among the universe of compounds it describes, or make the invention of the 220 Patent without extensive and time-consuming work. I find that the invention described in the 202 Patent is not disclosed in the 330 Patent, and therefore, it is not anticipated by it.

Obviousness

[84] In order for something to be an invention, it must be inventive or not obvious. The test for obviousness was set out by the Supreme Court of Canada in *Sanofi*. It observed that "obviousness is largely concerned with how a skilled worker would have acted in the light of the prior art." Accordingly, it instructed lower courts that an obviousness inquiry ought to follow a multi-step approach. The court should first identify the notional person skilled in the art. It should then identify the relevant common general knowledge of that person. The court next must identify the inventive concept of the claim in question or, if that cannot readily be done, construe it. With this information, the court must identify what if any differences exist between the prior art and the patent at issue. Lastly, and viewed without any knowledge of the patent at

issue, the court must ask whether those differences constitute steps which would have been obvious to the person skilled in the art or do they require a degree of inventiveness.

[85] The Defendants submit that the use of apixaban to treat and prevent thromboembolic disorders is obvious from the 330 Patent:

> A comparison of the claims of the 330 Patent and the claims of the 202 Patent show that the same uses for apixaban are covered in both, and apixaban is covered in both. That is, there is no difference between the prior art (330 Patent) and the claims of the 202 Patent. It is obvious that apixaban can be used to treat thromboembolic disorders as the 330 Patent states that the bicyclic compounds claimed therein (which include apixaban) are effective FXa inhibitors and are useful for the treatment of a thromboembolic disorder. [emphasis added]

[86] Contrary to the Defendants' submission, and as noted earlier, the experts testified that the skilled person reading the 330 Patent would expect that only a small percentage of the compounds therein described would be effective FXa inhibitors and useful to treat thromboembolic disorders. It would not be obvious to the skilled person that apixaban was included in the 330 Patent and even if it were, it would not be obvious that it was an effective FXa inhibitor useful in treating thromboembolic disorders as the evidence of Dr. Ohlstein confirms:

> Q. And if a person skilled in the art happened to pick out of the patent the compound apixaban somehow, and showed it to the skilled person, it would not have been self-evident that apixaban would be useful to treat thromboembolic disorders from looking at the 330 Patent and using their common general knowledge?
>
> A. I agree. Yes.

[87] Similarly, Dr. Gleason explained that to arrive at the conclusion that apixaban in the 330 Patent was useful to treat thromboembolic disorders, one would have to do what BMS did to find apixaban; namely, engage in complex, time-consuming, unpredictable research. I agree with BMS that the evidence shows that the "discovery of apixaban was the result of hard work, innovative thinking and a bit of good luck."

[88] For these reasons, the Defendants' submission that the subject matter of the invention set out in the 202 Patent was obvious from the 330 Patent fails.

Double Patenting

[89] Lastly, it is submitted by the Defendants that the 202 Patent is invalid because BMS has engaged in double patenting. They do not assert that the claims of the 202 Patent are identical or conterminous with those of the 330 Patent; rather they submit that the claims of the 202 Patent are not "patently distinct" from those of the 330 Patent. This is "obviousness-type" double patenting: See *Mylan Pharmaceuticals ULC v Eli Lilly Canada Inc*, 2016 FCA 119 [*Tadalafil FCA*] at para 28.

[90] The position of the Defendants is that the 202 Patent claims a compound covered by the 330 Patent for the same uses as were claimed in the 330 Patent, thus violating the prohibition on double patenting.

[91] The Federal Court of Appeal in *Tadalafil FCA* tells us that where an obviousness-type double patenting is being asserted, the Court must ask whether there is "invention" or

"ingenuity" in the move from the first patent to the second. If there is, then there is no double patenting.

[92] The Defendants assert that the "202 Patent does not define in clear terms the nature of a characteristic which BMS alleges to be possessed by apixaban compared to the prior group, so the 202 Patent is not 'patently distinct' from the 330 Patent." I disagree.

[93] As noted earlier, the 330 Patent describes an enormously large genus of compounds. Dr. Weitz testified that the skilled person would understand the 330 Patent to present an "aspiration" and that among the universe of compounds claimed; the skilled person understands the inventors hoped that there were effective FXa inhibitor compounds that had the "potential" to be therapeutically useful. The skilled person reading the 330 Patent knows that not all of its compounds would be FXa inhibitors effective in treating thromboembolic disorders. Specifically, the skilled person reading the 330 Patent would not know that apixaban was an FXa inhibitor effective in treating thromboembolic disorders.

[94] Dr. Gleason testified that the claims in the 330 Patent that the compounds are useful for treatment is based on a "prediction" that some compounds have the potential to treat thromboembolic disorders:

> Q. Yet, like your patent, this patent states that the compounds of the 330 Patent are all useful for treating thromboembolic disorders, and that, like yours, is a prediction made by the inventors based on the theory that if the compound inhibits factor Xa, it has the potential to treat thromboembolic disorders?
>
> A. That's correct.

> Q. And that is what the person of skill in the art would understand the inventors to be saying here, just like your patent, correct?
>
> A. That's correct.
>
> Q. Out of the vast expanse of compounds covered by this patent, those that inhibit factor Xa have the potential to treat?
>
> A. That's correct.
>
> Q. You agree that you can't predict based on structure alone whether a compound will be useful to treat a thromboembolic disorder, right?
>
> A. I would not be able to predict that because you cannot predict pharmacokinetics simply from structure.

[95] The prior patent, the 330 Patent, does not specifically identify apixaban as falling within its scope, although it is admitted that it does. More importantly, the 330 Patent does not inform the skilled person that apixaban will be useful in treating thromboembolic disorders. That result was obtained by BMS only after years of research and development. The discovery that apixaban could be used as an effective treatment of thromboembolic disorders was inventive.

[96] The evidence before the Court is that the skilled person reading the 202 Patent would know something that person would not know on reading the 330 Patent; namely, that apixaban is a FXa inhibitor effective in treating thromboembolic disorders. Dr. Gleason agreed with Dr. Weitz on this point:

> Q. So when a person skilled in the art looks at this patent and sees only one compound claimed, isn’t the likelihood they’re going to conclude that that compound is the one that’s useful to treat thromboembolic disorders?
>
> A. Yes.

[97] Ingenuity in the move from the 330 Patent to the 202 Patent is found. There is no double patenting.

Insufficiency and Inutility of a Selection Patent

[98] A selection patent is a patent whose subject matter is a small part of a large class that was the subject matter of another earlier patent. In this case, it is alleged that the 202 Patent is a selection patent, and the 330 Patent is the earlier patent. The Defendants submit that the 202 Patent, as a selection patent, is invalid because of "insufficiency and utility as a selection patent [emphasis added]."

[99] This submission relies on *In re I G Farbenindustrie A G's Patents* (1930), 47 RPC 289 (Ch D)] [*IG Farbenindustrie*] and the Supreme Court of Canada's discussion of it in *Sanofi* wherein at para 10, Justice Rothstein stated

> While not exhaustively defining a selection patent, he set out (at pp. 322-23) three conditions that must be satisfied for a selection patent to be valid.
>
> 1. There must be a substantial advantage to be secured or disadvantage to be avoided by the use of the selected members.
>
> 2. The whole of the selected members (subject to "a few exceptions here and there") possess the advantage in question.
>
> 3. The selection must be in respect of a quality of a special character peculiar to the selected group. If further research revealed a small number of unselected compounds possessing the same advantage, that would not invalidate the selection patent. However, if research showed that a larger number of unselected compounds possessed the same advantage, the quality of the compound claimed in the selection patent would not be of a special character.

[100] The explanation the court in *IG Farbenindustrie* gives for these three propositions, is critical to an understanding of what the court was actually saying about these propositions:

> The first proposition is plain (see the statement of Mr. Justice *Parker* in *Clyde Nail Co. Ld. v. Russell*, (1916) 33 R.P.C. 291, at 306). I will add that this condition must not be assimilated with the doctrine of utility as applied to an originating patent. In such a patent there may well be invention without utility. In a selection patent the condition that there must be a substantial advantage attributable to the use of the selected members is inherent in the so-called invention.
>
> The second proposition is derived from the circumstances that, the selection embraces selected members which do not possess the alleged advantages, the selection is defective and the patent would be misleading and would also fail for insufficiency and nonutility. It is not, however, intended to suggest that a few exceptions here and there would be regarded as invalidating the patent.
>
> The third proposition requires a little explanation. If there are five thousand possible members of the group, and one hundred have been selected as possessing some new and in definite advantage, is not intended to assert that such a selection patent would be bad if it was shown as a result of further research that there existed another hundred members possessing the same advantage. If, on the other hand, it were to be established there were a thousand unselected members which possess the same advantage, I doubt very much whether the patent could be sustained. The quality must be of the special character. It must not be one which those skilled in the art will expect to find in a large number of the members. It would be rash to attempt closer definition; the question is ultimately one of appreciation.
>
> ….
>
> I will summarize the conclusion which I have arrived by saying that in the selection patent the inventive step lies in the selection for a useful and special property or characteristic adequately defined…

[101] Having reviewed the reasons in *IG Farbenindustrie* and *Sanofi* and many of the Canadian authorities that reference *IG Farbenindustrie*, I conclude that there has often been a fundamental

misunderstanding of what Justice Maugham is saying. He, at page 322 (and Justice Rothstein at para 9 of *Sanofi* referencing the passage) clearly states that a failure to meet his three propositions regarding selection patents does not invalidate the patent; rather its validity is subject to the usual grounds relevant to any patent:

> Counsel on both sides have endeavoured in their able arguments to assist me by defining the conditions on which selection patents (if valid at all) can be supported. On consideration I think it would be unwise to endeavour to state in definite language all the conditions on which a selection patent must depend; for after all a selection patent does not in its nature differ from any other patent and is open to attack on the usual grounds of want of subject-matter, want of utility, want of novelty and so forth.

[102] Professor Norman Siebrasse in his blog "Sufficient Description" *Time to Relegate IG Farbenindustrie to the Dustbin of History* dated September 25, 2020, correctly notes that in *Sanofi*, the Supreme Court of Canada, when focusing on the validity of the patent there at issue, did not apply the propositions stated by Justice Maugham:

> [W]hile the SCC endorsed the *IG Farbenindustrie* requirements, it did not actually apply them in its analysis on the facts; the SCC relied on *IG Farbenindustrie* only for the proposition that "A system of genus and selection patents is acceptable in principle". Otherwise the SCC relied entirely on universally applicable principles of anticipation and obviousness.

[103] In my view, Justice Maugham's use of the word "valid" has led to this confusion. He is not stating that a selection patent must meet the three stated propositions to be a valid patent; rather he is saying that it must meet those three propositions to be a selection patent.

[104] The observation that failing to meet the three propositions does not in itself render the patent invalid, was noted by the Federal Court of Appeal in *Eli Lilly Canada Inc v Novopharm*

Ltd, 2010 FCA 197 [*Olanzapine FCA*] at para 33, where it was held that an examination of these three propositions is not a stand-alone basis to find a selection patent invalid:

> Novopharm referred to no authority, and I have not found any, where the analysis of the conditions for a valid selection patent, without more, has rendered a patent invalid. It is safe to say that the paucity of authority, considered in combination with my comments above, indicates that no such freestanding ground of attack exists. To reiterate, a determination that the conditions for a selection patent have not been met does not constitute an independent basis upon which to attack the validity of a patent. [emphasis added]

[105] Although the Defendants reference this passage from *Olanzapine FCA*, they go on to analyze the validity of the 202 Patent, as if these propositions were a stand-alone basis to invalidate the patent.

[106] In any event, I accept BMS's submission that if it were required to demonstrate compliance with the propositions in IG *Farbenindustrie*, the 202 Patent meets that test.

[107] As noted earlier, to the skilled reader, the 202 Patent does disclose special advantages of apixaban. Both Dr. Gleason and Dr. Weitz testified that the skilled person would understand that apixaban was singled out from the genus of compounds because, while the genus had the potential to be useful in treating thromboembolic disorders, apixaban was selected in the 202 Patent because it was useful. Thus disclosing its special advantage and distinguishing it from the others.

[108] The fact that BMS discovered two additional promising compounds does not invalidate the 202 Patent as a selection patent. As the Supreme Court of Canada noted in *Sanofi* at para 10,

"[i]f further research revealed a small number of unselected compounds possessing the same advantage, that would not invalidate the selection patent."

Conclusion on the 202 Patent

[109] For the reasons stated above, I find that none of the Defendants' grounds of attack on the 202 Patent succeeds. The Asserted Claims of the 202 Patent are valid.

THE 171 PATENT

[110] The claims of the 171 Patent at issue vary slightly in actions T-98-19 and T-503-19, with Claim 32 being at issue only in T-98-19. As earlier noted, the claims at issue are as follows:

> Court File No. T-98-19:
>
> > i. Claim 18 as it depends on claim 14, as it depends on either claim 13 or 12, as either depends on claim 6, as it depends on claim 5, as it depends on claim 4; and
> >
> > ii. Claims 30-32, as each depends on claim 29, as it depends on claim 25, as it depends on claim 24, as it depends on claim 23.
>
> Court File No. T-503-19:
>
> > i. Claim 18 as it depends on claim 14, as it depends on either claim 13 or 12, as either depends on claim 6, as it depends on claim 5, as it depends on claim 4; and
> >
> > ii. Claims 30-31, as each depends on claim 29, as it depends on claim 25, as it depends on claim 24, as it depends on claim 23.

[111] BMS's expert, Dr. Davies, was asked to focus on two groups of claims, as follows:

a) Claim Group A:

- 2.5 or 5 mg apixaban made from Form N-1 crystalline apixaban
- Prepared by dry granulation
- Having a D90 equal to or less than about 89 microns as measured by laser light scattering
- Dissolving at a rate of at least 77% within 30 minutes as determined by a USP Apparatus 2 at a paddle rotation speed of 75 rpm in 900 ml of a dissolution medium of 0.05 M sodium phosphate at a pH 6.8 containing 0.05% SLS at 37C

b) Claim Group B:

- Group A elements plus
  o Film coated tablets prepared by a specific dry granulation process (claims 24 and 25)
  o Formulation includes the excipients specified in claim 32

[112] The Defendants submit that issues of invalidity are to be measured against these claim elements and nothing else:

> It is in respect of these claim elements, and these claim elements alone, that issues of invalidity are to be assessed.
>
> Notably AUC, Cmax, "consistent in vivo exposures", "solution-like behaviour", "bioequivalence" and "therapeutic effect" are **not claimed**.

[113] These terms are all found in the disclosure. The Defendants submit that the claims are plain and unambiguous, and therefore recourse to the disclosure is not permitted to expand or limit the language of the claims. In support of that proposition, they reference two authorities.

[114] In *Electrical & Musical Industries Ld v Lissen Ld* (1939), 56 RPC 23 (HL) at 41, Lord Russell wrote:

> I would point out that there is no question here of words in Claim I bearing any special or unusual meaning by reason either of a dictionary found elsewhere in the Specification or of technical

> knowledge possessed by persons skilled in the art. The *prima facie* meaning of words used in a claim may not be their true meaning when read in the light of such a dictionary or of such technical knowledge; and in those circumstances a claim, when so construed, may bear a meaning different from that which it would have borne had no such assisting light been available. That is construing a document in accordance with the recognised canons of construction. But I know of no canon or principle, which will justify one in departing from the unambiguous and grammatical meaning of a claim and narrowing or extending its scope by reading into it words which are not in it; or which will justify one in using stray phrases in the body of a Specification for the purpose of narrowing or widening, the boundaries of the monopoly fixed by the plain words of a claim. [emphasis added]

[115] In *Pfizer Canada Inc v Canada (Minister of Health)*, 2007 FCA 209 [*Accupril FCA*] at para 39, Justice Nadon summarizes the principles set out by the Supreme Court of Canada in *Whirlpool* and *Free World Trust*:

> • The task of the Court is to construe the claims of the patent with the aid of expert witnesses (*Whirlpool* at paragraphs 43, 45 and 57).
>
> • Construction of the claims is not to be a result-oriented exercise and must be conducted by the Court prior to its consideration of the issue of infringement (*Whirlpool* at paragraphs 43 and 49(a)).
>
> • The claims are to be construed as of the publication date of the patent (*Whirlpool* at paragraph 42; *Free World* at paragraph 44).
>
> • In construing the claims of the patent, the Court is called upon to determine, on an objective basis, what a skilled reader would have understood the inventor to mean (*Whirlpool*, at paragraph 48; *Free World* at paragraph 51).
>
> • The claim of the patent which is to be construed by the Court must be read in the context of the rest of the specification. I would add to this, however, that reference to the rest of the specification cannot be used to expand the patentee's monopoly as expressed in the claim (*Whirlpool* at paragraphs 48, 49(f) and 52). [emphasis added]

> • The expert witnesses are there to help the Court understand the invention and its context, as well as the meaning of the terms used in the patent. Needless to say, it is the Court's duty to construe the claims and not that of the experts (*Whirlpool* at paragraphs 45 and 57).
>
> • In construing the claims, the Court is to keep in mind that the patent is addressed to the "ordinary person skilled in the art", i.e. a hypothetical person possessing the ordinary skill and knowledge of the particular art to which the invention relates, and a mind willing to understand a specification that is addressed to him (*Whirlpool* at paragraphs 53, 70, 71 and 74).
>
> • The "disclosure" found in the patent must describe the invention in a sufficiently complete and accurate manner so to allow the person skilled in the art to construct or use the invention when the period of monopoly has expired (*Whirlpool* at paragraph 42). The resulting construction of the claims should be one which is "in the interest of fairness both to the patentee and the public" (*Free World* at paragraph 50). As a result, the construction of the claim may lead to an expansion or limitation of the text of the claim. As Binnie J. said in *Free World* at paragraph 51:
>
> > 51. The involvement in claims construction of the skilled addressee holds out to the patentee the comfort that the claims will be read in light of the knowledge provided to the Court by expert evidence on the technical meaning of the terms and concepts used in the claims. The words chosen by the inventor will be read in the sense the inventor is presumed to have intended and in a way that is sympathetic to accomplishment of the inventor's purpose express or implicit in the text of the claims. However, 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.

[116] The Defendants rely primarily upon the underlined passages above in support of their submission. However, in both authorities, the courts recognize that what may seem clear and unambiguous may take on a different colour when the skilled person reads the claims in the

context of the whole specification. In this regard, the Federal Court of Appeal in *Mylan Pharmaceuticals ULC v Pfizer Canada Inc*, 2012 FCA 103 [*Aricept FCA*] at para 57 stated:

> The disclosure in the specification is to be understood from the viewpoint of a skilled person in the art or science to which the invention pertains, without resort to technicalities but rather for the purpose of seeking a construction of the claims which is reasonable and fair for both the patentee and the public: *Consolboard Inc. v. MacMillan Bloedel (Sask.) Ltd.*, [1981] 1 S.C.R. 504 at pp. 520-21. [emphasis added]

[117] In *Sanofi* at para 77, the Supreme Court of Canada observed that recourse to the specification is permissible when the inventive concept of the claims is not readily discernable from the claims:

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

[118] Similarly, in my view, a formulation patent may not disclose the inventive concept without recourse to the specification. While each step outlined in the claims of the 171 Patent may well be within the common general knowledge of a skilled formulator, this does not answer the question "what is the invention?"

[119] The invention was described by Dr. Davies in this way:

> [S]killed formulators reading the 171 Patent as a whole in light of their common general knowledge would have understood the inventive concept of both claim groups to be that 2.5 and 5 mg apixaban tablet formulations will provide solution-like and consistent *in vivo* exposures (thereby ensuring consistency in therapeutic effect) as long as:

> a. the formulation provides at least 77 wt% dissolution within 30 minutes when measured *in vitro* by the bio-relevant and discriminatory method set out in the patent's claims, and
>
> b. apixaban has a D90 of 89 µm or less.

[120] I do not accept the Defendants' characterization of Dr. Davies' opinion as being a "romp" through the disclosure. Nor do I accept their submission that he has altered the scope of the claims. Rather, he did what the Supreme Court of Canada in *Sanofi* at paragraph 67 said was the proper approach when conducting an obviousness inquiry; he compared the inventive concept with the state of the art:

> It will be useful in an obviousness inquiry to follow the four-step approach first outlined by Oliver L.J. in *Windsurfing International Inc. v. Tabur Marine (Great Britain) Ltd.* (1984), [1985] R.P.C. 59 (Eng. C.A.). This approach should bring better structure to the obviousness inquiry and more objectivity and clarity to the analysis. The *Windsurfing (1984)*, [1985] R.P.C. 59 (Eng. C.A.) approach was recently updated by Jacob L.J. in *Pozzoli SpA v. BDMO SA*, [2007] F.S.R. 37, [2007] EWCA Civ 588 (Eng. C.A.), at para. 23:
>
> > In the result I would restate the *Windsurfing* questions thus:
> >
> > (1)
> >
> > (a) Identify the notional "person skilled in the art";
> >
> > (b) Identify the relevant common general knowledge of that person;
> >
> > (2) Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
> >
> > (3) Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
> >
> > (4) Viewed without any knowledge of the alleged invention as claimed, do those differences constitute

> steps which would have been obvious to the person skilled in the art or do they require any degree of invention?
>
> [emphasis added.]

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

[121] While the Defendants' experts were not asked about the inventive concept of the patent, Dr. Kibbe in cross-examination accepted that if the two thresholds identified in the description were met, the tablet has solution-like behaviour and that was what the patent claims:

> Q. Let me remind you. I think you said on the one hand the inventors said if you meet the thresholds in the patent, you get tablets with solution-like behaviour that includes by observing the 89 micron D90 particle size specification. That's the one end of the dichotomy, right?
>
> A. That's what they claim, yes.
>
> Q. That's what the patent claims?
>
> A. Exactly.
>
> Q. And the skilled person would understand that reading the patent, correct?
>
> A. Would understand that that's what they claimed, yes.

[122] In short, I find that the Defendants' construction of the claims improperly ignores both the disclosure and the purpose of the two thresholds included in the asserted claims as essential elements. I find that the 171 Patent teaches that the claimed formulation is to be made observing the two thresholds, and doing so will ensure that the tablets provide consistent, solution-like exposures. One threshold is the minimum dissolution rate, and the other is a maximum particle size. Both thresholds are set out in the claims.

Obviousness

[123] The test for obviousness is set out above at paragraph 84.

[124] The Defendants submit that since this Court has sided with BMS in holding that the inventive concept must be considered, therefore "an examination of the Plaintiffs' invention story is necessary." They submit that the invention story offered by BMS "does not accord with the facts and does not support the inventive concept offered." They say that the invention story is "revisionist history" and offers no defence to a finding of obviousness. Alternatively, they say that the incentive concept of the asserted claims is obvious to try, and therefore invalid.

[125] Although the Defendants' submissions offered in the context of an invention story is creative, I prefer to examine the issue of obviousness using the *Windsurfing/Pozzoli* approach discussed earlier. I specifically reject as unfounded the submission that BMS has engaged in revisionist history.

Identify the Person Skilled in the Art

[126] It is agreed that the person skilled in the art is a formulator. I accept the Defendants' summary of the evidence of Dr. Davies, Dr. Laskar, and Dr. Kibbe as to the approach that a formulator takes in the drug development process:

> a) Take a conservative and risk-averse approach;
>
> b) Obtain a comprehensive understanding of the medicinal ingredient including conducting pre-formulation studies to determine a variety of characteristics and attributes such as

solubility, powder characteristics, excipient compatibility and hydrophobicity;

c) Formulate for the highest contemplated dose;

d) See solution-like behaviour as ideal for immediate release tablets;

e) Test to confirm the point at which the drug goes into solution;

f) Experiment with different methods and media in dissolution testing to develop a method that is discriminatory and representative;

g) Perform testing throughout the standard formulation development process such as dissolution testing, bioavailability studies, and site of absorption studies;

h) Consider data from (g) and make adjustments throughout development where results necessitate troubleshooting.

Identify the Relevant Common General Knowledge

[127] The 171 Patent teaches formulators how to make 2.5 and 5 mg apixaban tablet formulations in a way such that they will behave in the body as if it had been administered in a pre-dissolved liquid formulation. BMS, in closing, expressed the invention of the 171 Patent in this manner: “If you make those tablets in the way that the 171 Patent instructs, you are guaranteed to obtain tablets that provide consistent solution-like exposures.” We know other characteristics of the invention from the claims. The apixaban must have a D90 equal to or less than about 89 μm (i.e. 90% of the volume of particles in an apixaban composition have a diameter less than 89 μm). At least 77 wt% of apixaban must dissolve within 30 minutes (i.e. 77% of the drug dissolves within 30 minutes).

[128] The relevant common general knowledge at the claim date (February 25, 2010) is that dealing with particle size, dissolution rate, and known experiences with apixaban.

[129] Having reviewed the evidence of Dr. Davies, Dr. Laskar, and Dr. Kibbe, I agree with the submission of BMS as to the relevant common knowledge found at paragraphs 28 to 36 of its memorandum. The most relevant for this decision, are the following:

- Skilled formulators would have known that 2.5 and 5 mg apixaban doses are Class III drugs in the Biopharmaceutics Classification System (BCS), having high solubility and low permeability;

- Class III BCS drugs are expected to be permeability rate-limited and drug dissolution is expected to be irrelevant to absorption;

- Class III drugs are expected not to exhibit any *in vitro in vivo* correlation (IVIVC), and even if an IVIVC is found, it is expected to be limited and dissolution will not be rate-controlling;

- particle size – a factor that can influence drug dissolution – is not critical for BCS Class III drugs;

- particle size reduction is not a recognized formulation strategy for BCS Class III drugs like apixaban; and

- for Class III drugs, rapid dissolution of 85 % within 15 minutes in 0.1N HCl is the target for solution-like behaviour, and generally should not have any bioavailability problems.

Identify the Inventive Concept of the Claim

[130] The inventive concept of the 171 Patent is its teaching that if the apixaban tablet has a D90 equal to or less than about 89 µm and at least 77 wt% of apixaban dissolves within 30 minutes, then the tablets will provide consistent solution-like exposures.

What are the Differences between the State of the Art and the Inventive Concept?

[131] The state of the art was that a Class III drug like an apixaban tablet would behave like a solution if it achieved rapid dissolution of 85% within 15 minutes.

[132] As acknowledged by Dr. Laskar in the excepted passage below, and contrary to the state of the art, the skilled person reading the 171 Patent would understand that BMS discovered that 2.5 and 5 mg apixaban tablets do not need to meet that dissolution rate to behave like a solution. A much slower rate of dissolution of apixaban (77% within 30 minutes) achieves solution-like behaviour. Dr. Laskar confirmed that the state of the art was such that it was unexpected that at this much slower dissolution rate, solution-like behaviour would be observed:

> Q. Contrary to what the BCS and FDA have stated here, the inventors discovered and the 171 Patent discloses that two and a half and 5 milligram apixaban tablets do not need to provide fast or rapid dissolution to behave like a solution, correct?
>
> A. That is the assertion, yes.
>
> Q. And a skilled person would understand that, correct?
>
> A. They would understand the assertion, yes.
>
> Q. In fact the 171 Patent discloses that the tablets can provide far slower dissolution and still behave like a solution, correct?
>
> A. The authors of the patent assert that yes.

> Q. Right. In fact they can dissolve as slowly as 54 percent in 30 minutes in 0.1 normal HCl, correct? That's what's asserted in the patent, correct? Are you turning up the patent, Dr. Laskar?
>
> A. Yes. I'm looking at Table 5 A.
>
> Q. I think you should be looking at table 6A, Dr. Laskar.
>
> A. Okay. Will you repeat the question, please.
>
> Q. Yes, the 171 Patent discloses in table 6A that two and a half and 5 milligram tablets of apixaban can behave like a solution with far slower dissolution in 0.1 normal HCl than what Amidon in the 1997 FDA guidance recommends, correct?
>
> A. Are you referring to table 6A and the 85 percent in 15 minutes that's noted that their tablets A and C that are considered to be bioequivalent, as I recall, show what appear, what are slow dissolution rates in the point 1 normal HCl.
>
> Q. Far slower dissolution rates, correct?
>
> A. Far slower.
>
> Q. In fact, tablet B was used to establish the dissolution rate specification in the 171 Patent, correct?
>
> A. B was used, yes.
>
> Q. And at 30 minutes in 0.1 normal HCl it provided only 54 percent dissolution?
>
> A. That's correct.
>
> Q. I know we don't have a 15-minute time point, Dr. Laskar, but the dissolution in 0.1 normal HCl of tablet B would have been somewhere between 25 and 43 percent, correct?
>
> A. Yes, it would.

[133] I do not accept the Defendants' submission that the dissolution rate threshold set out in the 171 Patent is arbitrary. Paragraph 37 of the 171 Patent's disclosure correctly summarizes the evidence before the Court. It describes the results of clinical studies performed by BMS:

> The results of clinical studies demonstrated that, for tablets with similar dissolution rates (89% and 86% at 30 mm in pH 6.8 phosphate buffer containing 15 0.05% SLS), Cmax and AUC of the coated Phase 3 tablet (C) relative to the uncoated Phase 2 tablet (A), met bioequivalence criteria. Tablets with different dissolution rates (77% and 86% at 30 mm) had similar AUCs, but did not meet equivalence criteria for Cmax. The lower boundary of the 90% confidence interval of ratio of geometric mean Cmax was 0.788, indicating the rate of absorption, as defined by Cmax, was lower for the slower dissolving tablet (77% at 30 mm). Since the oral bioavailability from these tablets is shown to be comparable to that from solution (see figures 1 and 2 below), this dissolution rate (77% in 30 min) is defined as the threshold for achieving consistent exposure.

[134] Dr. Laskar in cross-examination admitted BMS had discovered something interesting; it discovered the point at which *in vitro* tablet dissolution started to affect Cmax. The exposures were independent of tablet dissolution above 77%, but 77% is the point at which tablet dissolution started to impact Cmax:

> Q. The inventors discovered the point at which *in vitro* dissolution started to impact Cmax, correct?
>
> A. They discovered a point at which, at which the Cmax was impacted by dissolution, yes.

[135] This evidence is sufficient to dispose of the assertion that the 77% threshold was an arbitrary selection made by BMS.

[136] The second threshold in the 171 Patent is particle size. Paragraph 38 of the 171 Patent's disclosure asserts that 89 µm was the largest particle size tested that did not exceed the minimum dissolution rate threshold for both 2.5 and 5 milligram doses. It was the maximum particle size

threshold and set as the threshold because “the oral bioavailability from tablets consistently matches that from solution.”

[137] The state of the art was that one would not expect to achieve any increased bioavailability by reducing particle size of a BCS Class III drug like apixaban. Dr. Laskar acknowledged in cross-examination that prior to the 171 Patent, particle size of a BCS Class III drug like apixaban should not be a critical factor when it comes to absorption exposure:

> Q. It says: "Such highly soluble drugs are advantageous in pharmaceutical development since no dissolution-enhancing principles are needed..." Pausing there. Do you agree with that statement?
>
> A. As a generality, yes.
>
> Q. And skilled persons would understand that as well?
>
> A. Yes, they would.
>
> Q. It carries on and says: "...and the process parameters that could affect drug particle form and size are generally not critical formulation factors." Correct?
>
> A. That's what's stated there, yes.
>
> Q. And skilled persons would have had that understanding as of the priority date of the 171 Patent, correct?
>
> A. As a generality, yes.

[138] Contrary to the common general knowledge, the inventors of the 171 Patent discovered that formulations made with large particles of apixaban resulted in less than optimal exposure. BMS says that it discovered the unobvious problem; namely, that a large particle size of apixaban can adversely affect *in vivo* exposure. As BMS notes, there may be an inventive step in recognizing that a problem exists at all: See *Cabot Corp v 318602 Ontario Ltd*, 1988

CarswellNat 569 at para 56 (Fed TD); *Glaxosmithkline Inc v Canada (Minister of Health)*, 2003 FC 899 at para 45; *Bayer AG v Novopharm Ltd*, 2006 FC 379 at para 44.

Do the Differences Require a Degree of Invention?

[139] Given the significant differences between the state of the art concerning BCS Class III drugs like apixaban, and the findings of the inventors, which were directly contrary to them, I have no hesitation in finding that a degree of invention was required to achieve the differences noted above.

[140] Further, I also have no hesitation in finding that what BMS did was not obvious to try. In *Sanofi* at paras 65 and 66 the Supreme Court held that the "obvious to try" test works only where it is very plain or more or less self-evident that what is being tested ought to work. In light of the prior art and common general knowledge, I am unable to find any evidence that convinces me on a balance of probabilities that it was more or less self-evident to try to obtain the invention, given the differences between the invention and the state of the art.

[141] For these reasons, the Defendants' invalidity challenge based on obviousness fails.

Insufficiency and Overbreadth

[142] The Defendants submit, "if a skilled person cannot know *a priori* whether her formulation has the claimed properties, the patent fails for insufficiency" and a "patent which claims more than the patentee disclosed or invented fails for overbreadth."

[143] They point to the cross-examination of Dr. Davies, saying that he admitted that "a skilled person cannot know the dissolution rate or particle size of a formulation without testing":

> Q. And to determine whether it has 77 percent dissolution rate, one needs to test?
>
> A. We always have to test the formulation, of course, because how would you know that it has 77 percent or more? Equally, you have to test the particle size. You'd always have to test.

[144] BMS points out that in *Apotex Inc v Merck & Co*, 2010 FC 1265 at para 532, Justice Snider observed that routine testing is permissible to work the invention and does not lead to a finding of the patent being insufficient:

> The courts have recognized that "routine trials and experiments not amounting to new inventions might be required to put [an invention] into practice" (*Procter & Gamble Co. v. Bristol-Myers Canada Ltd.* (1978), 39 C.P.R. (2d) 145 (Fed. T.D.) at para. 51, [1978] F.C.J. No. 812 (Fed. T.D.); see also, *Mobil Oil Corp. v. Hercules Canada Inc.* (1995), 63 C.P.R. (3d) 473, [1995] F.C.J. No. 1243 (Fed. C.A.)); *Aventis Pharma Inc. v. Apotex Inc.*, 2005 FC 1283, 43 C.P.R. (4th) 161 (F.C.) at para. 207).

[145] There is no evidence before the Court that the testing required is more than routine trial and experimentation. Indeed, in cross-examination Dr. Laskar admitted that a skilled formulator could reach into his or her "tool kit" and design a tablet that meets with the requirements of the 171 Patent. In short, I find that putting the 171 Patent invention into practice requires nothing more than the routine trials and experiments formulators use.

[146] The Defendants also assert that the 171 Patent's dissolution rate threshold is a mere desired result and submit that claims for desired results are invalid:

> [A patent that claims a desired result] fails to teach the skilled person how to obtain the invention, instead seeking to claim anything that achieves the claimed result. Such claims are both insufficient and all-encompassing (i.e. overbroad) at the same time.

[147] BMS notes that patent claims can also include functional limitations – claim elements essential to the purpose of the invention: *Burton Parsons Chemicals v Hewlett-Packard (Canada) Ltd*, 1972 CarswellNat 531 at para 24, (Fed TD), affirmed by the SCC which restored the trial judgment [1976] 1 SCR 555. I agree with BMS that the claims here are not as suggested by the Defendants. Rather, they are proper functional claims.

[148] For these reasons, I do not find that the 171 Patent is invalid for insufficiency or overbreadth.

Ambiguity

[149] A claim must be sufficiently explicit to inform the public as to what is within the claim and what is not within the claim. If a claim can be interpreted in more than one way such that it would be impossible for anyone to know in advance when a manufacture, use, or sale of the patented product would be within the claim, the claim is ambiguous, and invalid.

[150] The Defendants submit that the 171 Patent is ambiguous in claiming determination of particle size by "laser light scattering" with no instruction on the dispersion method to use. They say, "depending on the particular laser light scattering technique employed (wet dispersion versus dry dispersion) different particle size results are obtained."

[151] All of the experts who spoke about laser light scattering said that a formulator would know how to do it. For example, Dr. Kibbe's report states that "[t]he skilled Formulator would have also known how to measure the particle size of the API using a laser light scattering technique, as that method was commonly known and routinely used for this purpose in the pharmaceutical industry."

[152] I accept the evidence of Dr. Davis that done properly there is no difference between the wet and dry dispersion methods. Moreover, as he notes, the description of the 171 Patent disclosed that the inventor used the wet dispersion method and one working the invention would do the same:

> While Dr. Laskar points to this table as evidence that dry and wet dispersion will result in different measurements, this is not correct. In reality, what Table 7 and this document show is that, "the D90 for the milled API using LLS, wet dispersion method correlated well with those using LLS, dry dispersion method." When wet and dry dispersion techniques are used properly, this will generally be true.
>
> …
>
> Finally, if skilled formulators had any concerns about particle attrition, they would use wet dispersion, just like the inventors. In wet dispersion, a sample is dispersed in a liquid, which is far gentler and would be less likely to cause attrition. At paragraphs [0028] and [0029], the 171 Patent explains that the particle sizes determined and reported in the patent were determined using the wet dispersion technique. As set out in paragraph [0029], the apixaban materials were each measured three times (as required by the USP), and were placed in sample cells which were cleaned and filled with a suspending medium. This describes the wet dispersion technique, which almost always results in slightly larger particle sizes. <u>If there were any doubt, skilled persons would simply use wet dispersion</u>. [emphasis added]

[153] I therefore find that there is no ambiguity in the 171 Patent. The skilled person would know the dispersion method that had been used and would do the same when working the patent.

Inutility

[154] Lastly, and in the alternative to its submission on obviousness, the Defendants submit that the 171 Patent is invalid for lack of utility. Reading from paragraph 38 of the disclosure, they say that the practical purpose of the 171 Patent is stated to be that "controlling the particle size to less than 89 µm will result in a dissolution rate that will ensure consistent exposure."

[155] First, the Defendants submit that the criteria of controlling the D90 particle size to less than 89 µm did not show that one achieved a dissolution rate of 77% in 30 minutes thus ensuring consistent exposure. Secondly, they submit that the dissolution rate is arbitrary and meaningless in relation to the bioavailability of apixaban.

[156] In support of its first assertion, the inutility of the particle size on dissolution, they point to Table 6 in paragraph 36 of the 171 Patent, and the evidence of Dr. Kibbe. Dr. Kibbe's evidence at paragraph 319 of his report is that Table 6 refutes the assertion that using a D90 particle size equal to or less than 89 µm results in consistent dissolution:

> Tablets A and B of Table 6 were prepared using the same formulation, but Tablet A had a better dissolution rate than Tablet B (86 % versus 77%, in 30 minutes) despite having a larger D90 particle size (83.3 µm versus 53.1 µm). One would expect the inverse to be true, although the difference may be the result of scaling the formulation from a laboratory scale to a production scale.

[157] However, Dr. Laskar, the Defendants' expert, testified that the approach and conclusion of Dr. Kibbe looking at Table 6 was scientifically invalid as there were differences between these two tablets other than particle size – he was comparing apples to oranges:

> Q. Okay. So tablets A and B differed in both particle size and scale, correct?
>
> A. Yes, that's correct.
>
> …
>
> Q. Okay? Thank you. So it would be correct to say that more than one variable changed as between each tablet, correct?
>
> A. That would be correct.
>
> Q. In light of that, can we say that the difference in particle size caused the difference in the dissolution rate?
>
> A. No, we cannot. We cannot assign that as the, as a sole contributor. It may contribute, it may be one of the variables contributing, just as the other variables could also contribute.
>
> Q. We wouldn't be able to make that determination based on this information, correct?
>
> A. That is correct. We would not be able to assign.
>
> Q. Attempting to draw conclusions that it was the particle size that caused tablet B to dissolve more slowly would not be scientifically valid given that there were multiple changes or variable differences as between the tablets, correct?
>
> A. That's correct, and it would be, it would be counterintuitive to say that in as much as the D90 for B is smaller than that of tablet A, and given that the relationship between particle size and dissolution that, that the difference between A and B with respect to that would be counterintuitive.
>
> Q. And you can't draw that conclusion. It wouldn't be scientifically valid, correct?
>
> A. You cannot draw that as a conclusion.

[158] Moreover, Dr. Kibbe in cross-examination testified that one could not properly draw any conclusion from Table 6 about particle size and dissolution *in vitro*:

> Q. Okay. We were talking about multiple variables differing between the tablet formulations in Table 6. I think you said there were multiple differences, not just a single difference, correct?
>
> A. Right.
>
> Q. They differed in more than just particle size, correct?
>
> A. That's right. And so as we agreed, I think, you can't draw conclusions about the impact of particle size when you have lots of other things.
>
> Q. I think we are agreed that you cannot draw conclusions about the impact of particle size from the data in Table 6 and 6A. Correct?
>
> A. That's right.
>
> Q. Okay. And a skilled person would know that?
>
> A. Yes.
>
> Q. Right. In fairness, the patent is teaching or is directing a skilled person to Figures 3 and 4 as being where the patentee drew conclusions about the relationship between particle size and in vitro dissolution, correct?
>
> A. Yes.
>
> Q. The patent is not directing the skilled person to consider Table 6 and 6A to draw any conclusions about the impact of particle size on in vitro dissolution, agreed?
>
> A. That's right. And when you look at the particle size in 6 and 6A, you cannot draw a conclusion about it, except that there is no support for particle size predicting area under the curve from that set of data.
>
> Q. It would be improper to try and draw that conclusion from that set of data, correct?
>
> A. That's right. And therefore you cannot draw that conclusion.

> Q. Not only can you not, it would not be proper to do so, correct?
>
> A. You should not do that.

[159] For these reasons, I reject the Defendants' first submission on utility.

[160] The second submission is that the dissolution rate is arbitrary and meaningless in relation to the bioavailability of apixaban. As support, they point to the 019 study and say that therein a "tablet with 62 percent dissolution resulted in the same bioavailability as a tablet with 79 percent dissolution."

[161] This study is referenced at paragraph 35 and Table 5 of the 171 Patent. However, it is with reference to a 20 mg tablet and it compares the bioavailability of tablets produced by dry granulation and wet granulation processes. It states, "As shown in Table 5, the 20 mg tablets made using a dry granulation process had 79% apixaban dissolved in 30 minutes versus 62% apixaban dissolutive in 30 minutes made using a wet granulation process." As noted by BMS, the examples the Defendants rely on pertain to 20 mg BCS low solubility tablets that are not claimed in the Asserted Claims which are all directed to 2.5 and 5 mg BCS high solubility doses. I agree with BMS that accordingly, "Table 5 is irrelevant and does not reveal that the claimed formulations do not work."

[162] For these reasons, I also reject the Defendants' second ground of attack on the validity of the 171 Patent because of inutility.

Conclusion on the 171 Patent

[163] For the reasons stated above, I find that none of the Defendants' grounds of attack on the 171 Patent succeeds. The Asserted Claims of the 171 Patent are valid.

CONCLUSION

[164] The Defendants' allegations that their apixaban products will not infringe the 202 Patent or the 171 Patent, is based on their assertion that those patents are invalid. Having found that the Asserted Claims are valid, the relief sought by BMS in these actions shall issue. A copy of this Confidential Judgment and Reasons shall be filed and marked as confidential to the parties in each file.

[165] The parties touched only briefly on the issue of costs during their oral submissions. It was stated that BMS should be entitled to reduced or no costs if successful, because of statements made by counsel. I agree that the statements complained of were inappropriate but am of the view that they are not such that they impact BMS being entitled to its costs on the usual basis. If the parties are unable to agree on the amount of costs within 15 days of the issuance of these Reasons, they may make written submissions to the Court, not exceeding 20 pages, for the actions relating to the two patents in dispute. BMS is to provide its consolidated submissions within 30 days after the issuance of these Reasons, and each of the Defendants are entitled to respond within 15 days thereafter.

[166] The Reasons are being issued to the parties on a confidential basis. They have 15 days after the date hereof to advise the Court whether there is a requirement to redact any confidential information. The Public Judgment and Reasons shall be filed in each file.

JUDGMENT IN T-97-19, T-98-19, T-503-19 and T-504-19

THIS COURT'S JUDGMENT is that:

1. With respect to Canadian Patent No 2,461,202: Claim 2, Claim 4 as it depends on Claim 2, and Claims 5 to 7 as each depends on Claim 4, as it depends on Claim 2 [Asserted Claims of the 202 Patent in T-97-19 and T-504-19] are valid, and pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, it is hereby declared that the making, constructing, using or selling of apixaban tablets in accordance with Pharmascience Inc.'s submission for a Notice of Compliance for this drug as referenced in Pharmascience Inc.'s letter dated December 3, 2018, will directly or indirectly infringe at least one of the Asserted Claims of the 202 Patent in T-97-19 and T-504-19;

2. With respect to Canadian Patent No 2,461,202: Asserted Claims of the 202 Patent in T-97-19 and T-504-19 are valid, and pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, it is hereby declared that the making, constructing, using or selling of apixaban tablets in accordance with Sandoz Canada Inc.'s submission for a Notice of Compliance for this drug as referenced in Sandoz Canada Inc.'s letter dated February 8, 2019, will directly or indirectly infringe at least one of the Asserted Claims of the 202 Patent in T-97-19 and T-504-19;

3. With respect to Canadian Patent No 2,791,171: Claim 18 as it depends on Claim 14, as it depends on either Claim 13 or 12, as either depend on Claim 6, as it depends on Claim 5, as it depends on Claim 4; and Claims 30 to 32, as each depends on Claim 29, as it depends on Claim 25, as it depends on Claim 24, as it depends on Claim 23 [Asserted

Claims of the 171 Patent in T-98-19] are valid, and pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, it is hereby declared that the making, constructing, using or selling of apixaban tablets in accordance with Pharmascience Inc.'s submission for a Notice of Compliance for this drug as referenced in Pharmascience Inc.'s letter dated December 3, 2018, will directly or indirectly infringe at least one of the Asserted Claims of the 171 Patent in T-98-19;

4. With respect to Canadian Patent No 2,791,171: Claim 18 as it depends on Claim 14, as it depends on either Claim 13 or 12, as either depend on Claim 6, as it depends on Claim 5, as it depends on Claim 4; and Claims 30 to 31, as each depends on Claim 29, as it depends on Claim 25, as it depends on Claim 24, as it depends on Claim 23 [Asserted Claims of the 171 Patent in T-503-19] are valid, and pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, it is hereby declared that the making, constructing, using or selling of apixaban tablets in accordance with Sandoz Canada Inc.'s submission for a Notice of Compliance for this drug as referenced in Sandoz Canada Inc.'s letter dated February 8, 2019, will directly or indirectly infringe at least one of the Asserted Claims of the 171 Patent in T-503-19; and

5. Costs pursuant to subsection 6.12(1) of the *Patent Act* are reserved.

"Russel W. Zinn"
Judge

FEDERAL COURT

SOLICITORS OF RECORD

DOCKETS:	T-97-19 BRISTOL-MYERS SQUIBB CANADA CO ET AL v PHARMASCIENCE INC T-98-19 BRISTOL-MYERS SQUIBB CANADA CO ET AL v PHARMASCIENCE INC T-503-19 BRISTOL-MYERS SQUIBB CANADA CO ET AL v SANDOZ CANADA INC T-504-19 BRISTOL-MYERS SQUIBB CANADA CO ET AL v SANDOZ CANADA INC
PLACE OF HEARING:	HELD BY VIDEOCONFERENCE BETWEEN OTTAWA, ONTARIO AND TORONTO, ONTARIO
DATES OF HEARING:	SEPTEMBER 16-18, 21-25, 28-30, 2020 OCTOBER 1, 15, 16, 2020
JUDGMENT AND REASONS:	ZINN J.
CONFIDENTIAL JUDGMENT AND REASONS ISSUED:	JANUARY 4, 2021
AMENDED PUBLIC JUDGMENT AND REASONS ISSUED:	JANUARY 12, 2021

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