Federal Court Cour fédérale

Date: 20220706

Docket: T-555-20

Citation: 2022 FC 996

Toronto, Ontario, July 6, 2022

PRESENT: Madam Justice Pallotta

BETWEEN:

JANSSEN INC. AND
ACTELION PHARMACEUTICALS LTD

Plaintiffs

and

APOTEX INC.

Defendant

PUBLIC REASONS FOR JUDGMENT

(Judgment issued May 20, 2022 – 2022 FC 995)
(Confidential Judgment and Reasons issued May 20, 2022)

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I. **Overview**

[1] The plaintiffs, Janssen Inc. (Janssen) and Actelion Pharmaceuticals Ltd (Actelion), bring this patent infringement action against Apotex Inc. (Apotex) pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 [*PMNOC Regulations*], made under the *Patent Act*, RSC 1985, c P-4 [*Patent Act*].

[2] Janssen markets a prescription medication in Canada known as OPSUMIT®, a film-coated tablet containing 10mg of macitentan as the active ingredient, to treat patients afflicted with pulmonary arterial hypertension (PAH). PAH is a serious and incurable condition of high blood pressure in the blood vessels of the lungs, caused by changes to the arteries that transport deoxygenated blood from the heart to the lungs for reoxygenation. If left untreated, the high blood pressure strains the heart, leading to heart failure and death.

[3] OPSUMIT belongs to a class of drugs known as endothelin receptor antagonists (ERAs). ERAs work by binding to endothelin receptors within the walls of blood vessels, preventing endothelin from binding to these receptors. Endothelin binding is one of the steps in the endothelin pathway, a biological pathway that causes smooth muscle cells in blood vessel walls to constrict and proliferate, forcing the heart to work harder to push blood through the narrowed and thickened arteries. By blocking the endothelin binding step, ERAs interfere with the vasoconstricting and proliferative effects of the endothelin pathway.

[4] OPSUMIT can be prescribed alone or in combination with another class of drugs known as phosphodiesterase type-5 inhibitors (PDE5-Is). Like ERAs, PDE5-Is affect blood pressure,

but they do so by enhancing the vasorelaxation and anti-proliferative effects of the nitric oxide pathway. Sildenafil and tadalafil are two PDE5-Is prescribed for PAH.

[5] Currently, Janssen is the only company authorized by Health Canada to sell macitentan as a prescription medication. Apotex seeks Health Canada's approval to sell a generic prescription medication containing 10mg of macitentan as the active ingredient (APO-MACITENTAN).

[6] The plaintiffs allege that if Apotex sells APO-MACITENTAN, it will infringe claims 1-5, 10-20, and 21-31 (Asserted Claims) of Actelion's Canadian Patent No. 2,659,770 titled "Therapeutic Compositions Comprising a Specific Endothelin Receptor Antagonist and a PDE5 Inhibitor" (770 Patent).

[7] Claims 1, 10, and 21 are independent claims of the 770 Patent that relate to macitentan in combination with a PDE5-I to treat a disease wherein vasoconstriction is involved. The other Asserted Claims depend directly or indirectly on claims 1, 10, or 21, and they are narrower in scope. The dependent claims include limitations on the specific PDE5-I, the specific disease, or both.

[8] According to the plaintiffs, Apotex will infringe certain Asserted Claims directly, or indirectly by making statements in the APO-MACITENTAN product monograph (PM) that will induce others to infringe, notably prescribing physicians. With respect to inducement, the plaintiffs allege that the APO-MACITENTAN PM communicates that APO-MACITENTAN should not be used any differently than OPSUMIT. They allege the APO-MACITENTAN PM

includes bioequivalence data and results from a multicentre, double blind, placebo-controlled Phase 3 clinical trial (SERAPHIN) involving 742 PAH patients that established the safety and efficacy of macitentan as a monotherapy and as combination therapy with a PDE5-I. As such, the APO-MACITENTAN PM will encourage physicians to use APO-MACITENTAN just as OPSUMIT is used, in combination with PDE5-Is.

[9] For the purposes of this proceeding only, Apotex concedes that the Asserted Claims are valid. Apotex defends the plaintiffs' allegations on the basis that it will not infringe any of the Asserted Claims. Apotex alleges that it will not infringe any Asserted Claims directly because it will not perform all of the essential elements of the claims, and it will not infringe any Asserted Claims indirectly because the "Indications and Clinical Use" section of the APO-MACITENTAN PM states that [redacted] and the PM does not suggest that physicians or patients should use APO-MACITENTAN in combination with a PDE5-I.

[10] For the reasons below, the plaintiffs have not established that Apotex will directly infringe any of the Asserted Claims. The plaintiffs have established that Apotex will induce infringement of claims 1-5 and 21-31.

II. **Background**

A. *The Parties and the Nature of this Proceeding*

[11] Janssen is a pharmaceutical company with a head office in Toronto, Ontario. Actelion is a pharmaceutical and biotechnology company with a head office in Allschwil, Switzerland.

Janssen is wholly owned by Johnson & Johnson, which acquired Actelion in 2017. Both Janssen and Actelion are members of the Johnson & Johnson group of companies. Janssen is a "first person" within the meaning of subsections 4(1) and 6(1) of the *PMNOC Regulations*. Actelion is the registered owner of the 770 Patent and is a necessary party to this action under subsection 6(2) of the *PMNOC Regulations*.

[12] Apotex is a pharmaceutical corporation with its head office in Toronto, Ontario. Apotex is a "second person" within the meaning of subsections 5(1) and 6(1) of the *PMNOC Regulations*.

[13] Apotex filed an Abbreviated New Drug Submission (ANDS) with Health Canada, seeking authorization to market APO-MACITENTAN tablets based on their equivalent pharmaceutical and bioavailability characteristics, when compared to OPSUMIT.

[14] The Minister of Health maintains a list of patents related to drugs that have been authorized for sale under a notice of compliance (NOC). As a condition of obtaining market authorization for its macitentan product, the *PMNOC Regulations* required Apotex to address the patent list for OPSUMIT. Apotex served a Notice of Allegation on April 6, 2020 and the plaintiffs commenced this action in response.

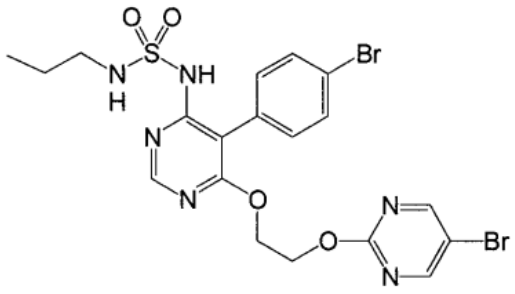
[15] When this action was commenced, three patents were listed in relation to OPSUMIT: Canadian Patent No. 2,437,675, Canadian Patent No. 2,621,273, and the 770 Patent. Canadian

Patent No. 2,437,675 has expired, and Canadian Patent No. 2,621,273 is not at issue in this action. Only the 770 Patent is at issue.

[16] By commencing this action, the plaintiffs triggered a stay that prevents the Minister of Health from issuing an NOC to Apotex for up to 24 months in order to allow time for the action to be heard and decided.

B. *The 770 Patent*

[17] The 770 Patent was issued on November 18, 2014. It relates to a specific compound, referred to throughout the patent as "formula (I)", in combination with a PDE5-I to treat diseases wherein vasoconstriction is involved. Formula (I) is identified by the following diagram of its chemical structure:



(I)

[18] There is no dispute that formula (I) is the compound now known as macitentan, the active ingredient in OPSUMIT, and that formula (I)/macitentan is an ERA.

[19] The first paragraph of the 770 Patent specification describes the invention as relating to a product containing a compound of formula (I) in combination with at least one compound having

PDE5-inhibitory properties for therapeutic use in the treatment of a disease wherein vasoconstriction in involved. The specification states that "disease wherein vasoconstriction is involved" means in particular hypertension, pulmonary hypertension (including PAH), diabetic arteriopathy, heart failure, erectile dysfunction or angina pectoris. Some of the Asserted Claims do not include a limitation on the particular disease wherein vasoconstriction is involved, while others are limited to: the particular diseases of vasoconstriction listed above, hypertension and pulmonary hypertension, pulmonary hypertension (PH) specifically, or PAH specifically.

[20] The patent specification defines "compound having PDE5-inhibitory properties" to be a compound that meets or exceeds a threshold measurement of its ability to inhibit PDE5 according to an experimental test protocol described in the patent, and it provides four examples of PDE5-Is: sildenafil, vardenafil, tadalafil, and udenafil. Some of the Asserted Claims do not include a limitation on the PDE5-I, and others are limited to: the four example PDE5-Is, sildenafil or tadalafil, sildenafil specifically, or tadalafil specifically.

C. *PAH and Diseases Involving Vasoconstriction*

[21] Vasoconstriction is the constriction of the vasculature (arteries and veins) of the circulatory system. The vasculature can be divided into two systems that circulate blood between the body, heart, and lungs. The systemic circuit involves the left side of the heart, which pumps oxygenated blood from the heart to the rest of the body (except the lungs). The pulmonary circuit involves the right side of the heart, which pumps deoxygenated blood from the heart to the lungs for reoxygenation.

[22] Although some of the Asserted Claims cover other diseases of vasoconstriction and are not limited to PAH, PAH is the only disease that is relevant to the issues in this action because the allegations of direct and indirect infringement are restricted to PAH.

[23] PAH is a subtype of PH, a general term that describes abnormally high blood pressure in the pulmonary circulatory system. As noted above, PAH is a progressive and incurable disease where the artery walls in the lungs constrict and thicken, increasing vascular resistance to blood flow and making the right side of the heart work harder to push blood through narrowed arteries. The extra stress causes the right ventricle of the heart to enlarge and dilate. Over time, the changes become unsustainable. The right ventricle weakens, its ability to push blood out of the heart to the lungs is compromised, and eventually, the heart fails.

III. **Issues**

[24] The issues in this action relate to claim construction and infringement of the Asserted Claims. As noted above, validity of the 770 Patent is not an issue that is before the Court.

[25] The Asserted Claims of the 770 Patent must be construed—that is, interpreted—before there is an assessment of whether they are infringed: *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at para 43 [*Whirlpool*]. Doing so requires that the claims be read in an informed and purposive way, from the perspective of a notional person of ordinary skill in the art or science to which the patent relates, and to whom the patent is addressed (skilled person): *Free World Trust v Électro Santé Inc*, 2000 SCC 66 at para 44 [*Free World*].

[26] While the parties in this case and their expert witnesses largely agree (with some variation) on the qualifications of the skilled person and the relevant experience and knowledge that person would bring to bear on the issues in the action, the first issue for the Court is to define the skilled person.

[27] The parties filed a joint claim chart. Despite their identical proposed constructions of the essential elements of the Asserted Claims, the parties do not agree on what the claims mean. Two aspects of claim construction are in dispute: (i) whether claims 1, 10 and their dependent claims are, in substance, claims to the use of macitentan to treat a disease including PAH; and (ii) for all Asserted Claims, whether "combination" contemplates the use of macitentan and a PDE5-I as something that a physician intended at the outset of a patient's treatment.

[28] The Court's claim construction analysis is not confined to the aspects of claim construction that are in dispute. The Court is not required to accept the parties' or the experts' proposed claim construction. Claim construction is a matter of law for the Court to decide: *Whirlpool* at para 61; *Zero Spill Systems (Int'l) Inc v Heide*, 2015 FCA 115 at para 41 [*Zero Spill*]. The construction of the Asserted Claims is the second issue.

[29] The application for the 770 Patent was published on March 6, 2008. This is the relevant date for construing the claims: *Free World* at paras 53-54. The skill and knowledge that the skilled person brings to bear when interpreting the claims is their skill and knowledge as of March 6, 2008. For simplicity, I will sometimes refer to the 770 Patent's publication date as March 2008 or I will refer to the year only.

[30] The plaintiffs bear the burden of proving infringement on a balance of probabilities. The parties' joint statement of issues frames the infringement issue as follows:

> The Court will be required to decide whether, if approved, the making, constructing, using, or selling of APO-MACITENTAN 10 mg film-coated tablets, by Apotex Inc. in accordance with its Abbreviated New Drug Submission No. 2365227 constitutes infringement of any of the Asserted Claims of the 770 Patent, either directly or indirectly by inducing others to infringe.

[31] As the third issue, the Court must decide whether the plaintiffs have established that Apotex would directly infringe claims 1-5 and 10-20, if it is authorized to market APO-MACITENTAN.

[32] As the fourth issue, the Court must decide whether the plaintiffs have established that Apotex would indirectly infringe claims 1-5 and 21-31 by inducing others, notably prescribing physicians, to infringe. As noted above, the plaintiffs assert that statements made in the APO-MACITENTAN product monograph (PM) will induce prescribing physicians to infringe the Asserted Claims.

[33] At the outset of trial, the plaintiffs stated that they were alleging Apotex would infringe claims 10-20 indirectly, however, their written closing argument did not address indirect infringement of claims 10-20. In view of my construction of claims 10-20, I would not have found indirect infringement for these claims.

IV. **Witnesses**

[34] Each of the parties introduced expert evidence in support of their respective positions on claim construction and infringement. The plaintiffs relied on the expert opinion evidence of Dr. Mielniczuk and Dr. Kapasi. Apotex relied on the expert opinion evidence of Dr. McIvor and Ms. Picard.

[35] The parties agree on a number of facts. As a result, neither party called fact witnesses. They provided a joint scientific primer and an agreed statement of facts.

[36] That said, the plaintiffs submit that Apotex should have called a fact witness from the company. They argue an adverse inference should be drawn because the only evidence regarding Apotex's actions and intentions—which are centrally important to the issue of infringement—was Dr. McIvor's and Ms. Picard's speculation. The plaintiffs therefore argue that this Court should infer that Apotex did not call a company witness because their evidence would not have been helpful to Apotex's position.

[37] I decline to draw an adverse inference based on Apotex's alleged failure to call a company witness. According to the joint statement of issues, the question on infringement is whether the making, constructing, using or selling of APO-MACITENTAN in accordance with Apotex's ANDS would constitute direct or indirect infringement. In this regard, the plaintiffs asked Drs. Mielniczuk and Kapasi to review the proposed APO-MACITENTAN PM and product label that Apotex submitted as part of its ANDS, and opine on: (i) how APO-MACITENTAN will be used by physicians and patients if it is approved, sold, and used in

Canada; and (ii) what Apotex's influence will be on the use of APO-MACITENTAN in Canada by physicians and patients. Both experts opined that Apotex would represent that APO-MACITENTAN can be used in place of OPSUMIT through the information within the proposed APO-MACITENTAN PM.

[38] The following provides a brief description of each expert witness' qualifications and testimony.

A. *Dr. Mielniczuk (Plaintiffs' Expert Witness)*

[39] Dr. Mielniczuk is a Staff Cardiologist and Medical Director of the Pulmonary Hypertension Clinic at the University of Ottawa Heart Institute. She has been in this role since 2007. Dr. Mielniczuk received her M.D. from McMaster University in 1998. She completed a residency in internal medicine at Queen's University in 2001, and a fellowship in cardiology at the University of Ottawa Heart Institute in 2004. Dr. Mielniczuk also completed a fellowship in advanced heart failure and cardiac transplantation at the Brigham and Women's Hospital in Boston, Massachusetts in 2006. She received a Master of Science degree in Clinical Science and Epidemiology from the Harvard School of Public Health in 2007.

[40] Dr. Mielniczuk's research activities focus on heart failure, clinical outcomes relating to heart failure associated with PH, and the evaluation of myocardial energetics in right heart failure.

[41] Apotex did not object to Dr. Mielniczuk's proposed qualifications. I was satisfied Dr. Mielniczuk was qualified to provide expert evidence according to the proposed qualifications that were put forward by the plaintiffs:

> Dr. Mielniczuk is a medical doctor, researcher, and professor of cardiology with expertise in (i) pulmonary hypertension ("PH") (including pulmonary arterial hypertension ("PAH")); (ii) the development and science of treatment of PH (including PAH); and (iii) the treatment of PH (including PAH) in Canada, past and present.

[42] Dr. Mielniczuk prepared an expert witness report dated July 15, 2021. The report sets out Dr. Mielniczuk's opinions on mandates related to the qualifications and knowledge of the skilled person, construction of the Asserted Claims, how PAH is treated today, how APO-MACITENTAN will be used by physicians and patients in Canada, and what Apotex's influence will be on the use of APO-MACITENTAN by physicians and patients. Dr. Mielniczuk's report was taken as read.

B. *Dr. Kapasi (Plaintiffs' Expert Witness)*

[43] Dr. Kapasi is an Associate Professor of Medicine at the University of British Columbia. Dr. Kapasi received his M.D. from the University of Alberta in 2003 and completed a residency in family medicine in 2004. He also completed a residency in internal medicine at the University of Manitoba in 2006, a respirology subspeciality training program in 2008, and a fellowship in lung and heart/lung transplantation in 2009. Dr. Kapasi received a Masters in Pulmonary Vascular Disease from the Università di Bologna in 2012.

[44] Since the beginning of his practice of medicine in 2009, Dr. Kapasi's focus has been on treating cardiovascular diseases, with a particular interest in diseases affecting the pulmonary circulatory system.

[45] The plaintiffs proposed that Dr. Kapasi be qualified to testify as an expert as follows:

> Dr. Kapasi is a medical doctor, researcher, and professor of pulmonary medicine with expertise in (i) pulmonary hypertension ("PH") (including pulmonary arterial hypertension ("PAH")); (ii) the development and science of treatment of PH (including PAH); and (iii) the treatment of PH (including PAH) in Canada, past and present.

[46] Apotex did not object to the proposed qualifications, and I was satisfied that Dr. Kapasi was qualified to provide expert testimony in accordance with the proposed qualifications.

[47] Dr. Kapasi prepared an expert witness report dated July 15, 2021. Dr. Kapasi's report covered his opinions on the same mandates as Dr. Mielniczuk's report. Dr. Kapasi's report was taken as read.

[48] Prior to Dr. Kapasi's testimony at trial, Apotex registered an objection to Dr. Kapasi's expert opinion evidence on the ground that his evidence is duplicative of Dr. Mielniczuk's expert opinion evidence. Having noted the objection, Apotex stated that it would provide its submissions on the objection in the context of closing arguments.

[49] Apotex did not provide submissions on the objection in its written or oral closing arguments. Following a question from the Court, asking whether the objection was withdrawn,

Apotex stated it was not objecting to the admissibility of Dr. Kapasi's expert opinion evidence but it reserved the right to speak to the issue on costs. Apotex then added that the duplicative nature of the evidence should be a factor considered in assigning weight to Dr. Kapasi's evidence, and the plaintiffs raised an objection. The plaintiffs' position was that, having made no submissions in its closing arguments (and in fact, Apotex relied on both Dr. Kapasi's and Dr. Mielniczuk's evidence on various points), and having withdrawn the objection, it was not open to Apotex to argue that Dr. Kapasi's opinion should be given less weight because it is duplicative. In any event, the plaintiffs submit Dr. Kapasi's and Dr. Mielniczuk's opinions are corroborative rather than duplicative.

[50] Apotex argued that an opinion from a second, similarly-situated PAH expert does not assist the Court according to the framework set out in *R v Mohan*, [1994] 2 SCR 9. In my view, that is a question of admissibility, and Apotex stated it was not objecting to the admissibility of Dr. Kapasi's evidence. Apotex also argued that the Court should not decide issues on the basis that two experts are better than one. In my view, that caution was unnecessary. I have not given "extra weight" to the opinions of either of the plaintiffs' experts simply because there were two of them.

C. *Dr. McIvor (Apotex's Expert Witness)*

[51] Dr. McIvor is a respirologist (also referred to as a pulmonologist, especially in the United States) whose clinical practice and research focuses on a range of respiratory disorders. Dr. McIvor was trained in internal medicine in the United Kingdom from 1984 to 1989, and enrolled in the Respirology Training Program at the University of Toronto from 1990 to 1992. Dr.

McIvor received his M.D. from Queen's University in Belfast, Northern Ireland in 1994 and a Master of Science degree in clinical epidemiology from McMaster University in 1995. Since 2005, he has been a Staff Respirologist at the Firestone Institute for Respiratory Health (FIRH) of St. Joseph's Healthcare Hamilton and a Professor of Medicine at McMaster University. FIRH is a referral centre for patients in the Hamilton Area with asthma and chronic respiratory disease, including patients with PAH.

[52] Dr. McIvor was qualified to testify as an expert as follows:

> Dr. McIvor is a respirologist with expertise in the diagnosis, management and treatment of respiratory conditions including Pulmonary Arterial Hypertension.

[53] Dr. McIvor prepared an expert witness report dated October 12, 2021. The report sets out Dr. McIvor's opinions on mandates related to the qualifications and knowledge of the skilled person, construction of the Asserted Claims, how PAH is treated today, how a physician would understand the instructions from the APO-MACITENTAN PM, whether the PM would result in direct infringement or induce physicians to infringe the Asserted Claims, and responses to Dr. Mielniczuk and Dr. Kapasi's reports. Dr. McIvor's report was taken as read.

D. *Ms. Picard (Apotex's Expert Witness)*

[54] Ms. Picard is a pharmacist and President of SPharm Inc., a regulatory consulting firm that provides strategies and consultancy to pharmaceutical companies. She has a Master's degree in hospital pharmacy and 30 years of experience in regulatory affairs.

[55] Ms. Picard prepared an expert report dated October 12, 2021. Ms. Picard was asked to provide her opinion on whether Apotex would be permitted to market or promote that APO-MACITENTAN can be used as a combination therapy with PDE5-Is, based on the APO-MACITENTAN PM provided to her. She was also provided with copies of Dr. Kapasi's and Dr. Mielniczuk's reports and asked to comment on those portions of their expert reports relevant to her expertise, and advise whether she agreed or disagreed.

[56] Apotex proposed the following qualifications for Ms. Picard:

> Susanne Picard is a licensed pharmacist and an expert in Canadian pharmaceutical regulatory affairs, including the preparation, filing and management of new and abbreviated new drug submissions. She has particular expertise in: (a) the preparation and filing and interpretation of brand and generic Product Monographs ("PMs"); (b) the relevant regulations and guidelines for preparing PMs; (c) Health Canada's evaluation of PMs; and (d) the regulations applicable to the marketing of approved pharmaceuticals.

[57] At trial, the plaintiffs objected to Ms. Picard's proposed qualifications. After hearing the parties' arguments, I revised the proposed qualifications offered by Apotex by deleting the word "particular" from the second sentence and adding a proviso. These changes were intended to make it more explicit that Ms. Picard's opinions offer one perspective of PMs, the regulations and guidelines, and Health Canada's evaluation of PMs, and her opinions do not go further than that perspective. The revised statement of qualifications is as follows:

> Susanne Picard is a licensed pharmacist and an expert in Canadian pharmaceutical regulatory affairs, including the preparation, filing and management of new and abbreviated new drug submissions. She has ~~particular~~ expertise in: (a) the preparation and filing and interpretation of brand and generic Product Monographs ("PMs"); (b) the relevant regulations and guidelines for preparing PMs; and (c) Health Canada's evaluation of PMs; and (d) the regulations applicable to the marketing of approved pharmaceuticals, provided

> that the expertise noted as (a), (b), (c), and (d) is within Ms. Picard's expertise as a pharmacist or in Canadian pharmaceutical regulatory affairs.

[58] The plaintiffs also argued that most parts of Ms. Picard's expert report (paragraphs 23, 24, 53, 55-60 and 62-80) are inadmissible. These are almost all of the paragraphs in Ms. Picard's report that provide an opinion on the APO-MACITENTAN PM. The remaining paragraphs in the report provide information about Ms. Picard's qualifications, or information about the regulations made under the *Food and Drugs Act* and other aspects of the regime that governs drug marketing in Canada.

[59] The plaintiffs do not take issue with Ms. Picard's qualifications as an expert in the area of regulatory affairs; however, they say her expertise in this regard is irrelevant to the issues in this case and does not support most of the opinions within her expert report. The plaintiffs object to the above-noted paragraphs principally on two bases: (i) Ms. Picard provides opinions that are outside her expertise; and (ii) Ms. Picard provides opinions on domestic law, which should be excluded for that reason and also for being unnecessary.

[60] According to the plaintiffs, Ms. Picard is not a properly qualified expert whose opinion is relevant and necessary to assist the Court: *White Burgess Langille Inman v Abbott and Haliburton Company Limited*, 2015 SCC 23. All drafts of the PM that were submitted to Health Canada are already in evidence, Ms. Picard's interpretation of them from the perspective of a regulatory affairs expert are not relevant to inducement, and she cannot provide the perspective of a PAH physician. Also, Ms. Picard is not a lawyer and the Court does not need her evidence to take judicial notice of the *Food and Drugs Act* or the regulations thereunder. The plaintiffs

further note that Ms. Picard's opinions on what Apotex can and cannot do from a regulatory perspective are not grounded in fact evidence from Apotex, and she does not know its marketing plans.

[61] The plaintiffs say the situation is analogous to *Bell Helicopter Textron Canada Limitée v Eurocopter*, 2013 FCA 219. In that case, the Court ruled that an expert's opinion on the patent examination process before the Patent Office was irrelevant because the expert had no expertise on the technology in question, the patent examination history was already in evidence, a patent examiner's perspective was irrelevant to the Court's assessment of validity from a skilled person's perspective, and expert opinion on domestic law was unnecessary.

[62] Apotex's responding position was that the Court should reserve on the question of admissibility, but if the Court were inclined to rule on admissibility during the trial, Ms. Picard's evidence met the test for admissibility as expert opinion.

[63] On the first point, Apotex argued that a determination of admissibility at trial would be premature. There was insufficient reason to rule that parts of Ms. Picard's report should be excluded based on the threshold requirements of admissibility, and no reason to engage the Court's discretionary gatekeeper role of balancing the potential risks and benefits of admitting her evidence. A central issue in this action relates to Apotex's intentions as gleaned from an objective reading of the PM, and Ms. Picard's experience allows her to opine on what can be inferred from the PM based on the purpose of a PM and the regulatory framework that applies to it. Apotex argued it would be efficient to allow Ms. Picard to testify under reserve of objection,

and doing so would also promote fairness because Apotex did not have advanced notice of the challenged paragraphs and the bases for objecting to them.

[64] On the second point, Apotex argued that Ms. Picard's evidence meets the threshold requirements for admissibility, and the plaintiffs' objections should be considered as a matter of weight. The regulatory perspective of an expert who provides advice to pharmaceutical companies on PMs and the marketing of a drug product is helpful to assist the Court in understanding the PM. Although guided by legislation, Ms. Picard's evidence is not a legal opinion and her evidence should not be excluded on this basis. Ms. Picard can assist the Court to navigate a complex regime that involves an interplay between legislation, standards, guidance documents, and other considerations.

[65] I agreed with Apotex that it was premature to rule on admissibility at trial. It was not clear to me that all of the impugned paragraphs should be excluded as inadmissible on the basis of relevance or necessity, and I reserved my ruling on admissibility.

[66] As noted above, as her first mandate Ms. Picard was asked to provide her opinion on whether Apotex would be permitted to market or promote that APO-MACITENTAN can be used as a combination therapy with PDE5-Is, based on the APO-MACITENTAN PM provided to her. As her second mandates she was provided with copies of Dr. Kapasi's and Dr. Mielniczuk's reports and asked to comment on those portions of their expert reports relevant to her expertise, and advise whether she agreed or disagreed.

[67] With respect to the second mandate, I find Ms. Picard's expert report and testimony to be inadmissible because her opinions are outside of her expertise. For example, Ms. Picard offered opinions on whether or not the references to SERAPHIN found in the APO-MACITENTAN PM would support the use of macitentan as a monotherapy or as combination therapy. Ms. Picard is not qualified to do so as she is not a physician, she has no expertise regarding PAH, and she is not qualified to opine on whether the APO-MACITENTAN PM "omits any discussion of efficacy as it relates to the use of combination therapy". Her opinion in this regard was based on a side-by-side comparison of words deleted from the APO-MACITENTAN PM. This is an exercise of form over substance that is potentially misleading from an expert witness with no PAH expertise.

[68] With respect to the first mandate, and to the extent that Ms. Picard's evidence fell within the scope of her expertise as a pharmaceutical regulatory expert, I find the opinions have marginal relevance to the issues that the Court must determine in this case. For example, Ms. Picard provided a generalized opinion that generic pharmaceutical companies are not free to omit clinical and pre-clinical studies that are included in a PM for the "reference product" (the brand company's PM) because these studies are typically conducted to establish the safety and/or efficacy of the drug in question. However, Ms. Picard has no knowledge about what Apotex was or was not required to include from SERAPHIN in particular. As another example, Ms. Picard opined that Apotex would not be permitted to market or promote that APO-MACITENTAN can be used as a combination therapy with PDE5-Is, based on the APO-MACITENTAN PM provided to her. However, the issue in this case is whether the contents of the APO-

MACITENTAN PM itself would induce physicians to infringe. I accord these opinions little weight.

V. **The Skilled Person and Their Common General Knowledge**

[69] The notional person of skill in the art or "skilled person" is a legal construct embodying a number of concepts that inform a proper approach to resolving issues of claim construction, infringement, and validity in a patent action.

[70] The skilled person possesses a level of skill and knowledge necessary to appreciate the nature and description of the invention at a technical level: *Whirlpool* at para 53. This is the ordinary level skill of and knowledge of the particular art or science to which the patent relates: *Free World* at para 44. The skilled person embodies the "common general knowledge" (CGK) that is generally known and accepted in the field, and they are reasonably diligent in keeping up with advances: *Pfizer Canada Inc v Teva Canada Limited*, 2017 FC 777 at para 185.

[71] Where a patent relates to multiple scientific or technical fields, the skilled person can comprise a team of people: *Amgen Inc v Pfizer Canada ULC*, 2020 FC 522 at para 172. However, the skilled person is not defined on a claim-by-claim basis: *Teva Canada Limited v Janssen Inc*, 2018 FC 754 at para 236, aff'd 2019 FCA 273, leave to appeal to SCC refused, 39007 (7 May 2020).

[72] Expert witnesses assist the Court by opining on the qualifications, relevant experience and knowledge of the notional skilled person, and how to assess the issues in dispute from the

skilled person's frame of reference in view of the relevant experience and knowledge they would bring to bear: *Tetra Tech EBA Inc v Georgetown Rail Equipment Company*, 2019 FCA 203 at para 88, citing *Free World* at para 51.

[73] Drs. Mielniczuk and Kapasi opine that the 770 Patent focuses on the use of macitentan in combination with a PDE5-I to treat a disease where vasoconstriction is involved, particularly PH and PAH. Therefore, the skilled person would be a cardiologist, pulmonologist, or general internist who is capable of identifying and diagnosing PH and PAH, and is capable of either providing direct treatment or referring patients to the appropriate specialist. Dr. Kapasi adds that the skilled person may be part of a larger team that includes those with expertise in pre-clinical animal studies and pharmacology, and an interest in researching diseases related to the circulatory system.

[74] Dr. McIvor opines that the skilled person is a physician with experience in treating patients in diseases wherein vasoconstriction is involved, including PAH. Since severe respiratory diseases, such as PAH, are treated by specialists, the skilled person would have specialized training. The skilled person would have several years of practical clinical experience, as well as experience with or knowledge of the design of clinical trials and the interpretation of their results.

[75] While Dr. McIvor notes that parts of the 770 Patent are directed to those with experience in formulating pharmaceutical products and/or preclinical experiments, he adopted the perspective of the skilled person having the skill set of a physician.

[76] Ms. Picard did not provide an opinion on the skilled person. In these Reasons, references to "physician experts" mean Drs. Mielniczuk, Kapasi, and McIvor.

[77] In this case, the parties and the physician experts have focused on the skilled person's qualifications as a physician who would treat PH and PAH and in this regard, they do not materially disagree on the skilled person's qualifications. While the 770 Patent is not limited to PH or PAH, based on statements in the specification that the disease intended to be treated is "more preferably" selected from hypertension and PH, "in particular" PH, and "notably" PAH, I accept that the 770 Patent is more focused on hypertension and PH. Furthermore, I accept that treatment decisions and the management of patients with PAH are made by specialists having an understanding of PH and PAH. In my view, the skilled addressee of the 770 Patent would have knowledge and skills related to the treatment of diseases of vasoconstriction generally, but the skilled person would also have the specialized knowledge about PH or PAH and its treatments.

[78] Dr. Mielniczuk's and Dr. Kapasi's reports summarize the skilled person's CGK as of 2008 regarding PH and PAH, including diagnosing and treating PAH in view of the diagnostic methods and treatments that were available at the time. Their main points are:

a) PAH is a subgroup of PH, characterized by elevated blood pressure in the pulmonary arteries due to a progressive remodeling and narrowing of the arterial walls;
b) The severity of a patient's symptoms were graded according to a functional classification scheme developed by the World Health Organization (WHO); functional classes I-IV described progressive levels of incapacity and served to monitor disease progression and to inform the therapeutic approach;

c) PAH was rarely diagnosed early: patients often delayed seeking treatment because symptoms progress gradually; the diagnosis was often delayed because PAH symptoms can be attributed to more common cardiorespiratory diseases, and co-morbidities (particularly in older patients) can mask the disease; as a result, PAH was often diagnosed after other possibilities had been ruled out, and it was typically diagnosed in younger patients, particularly otherwise healthy young women;
d) By the time most patients began receiving treatment for PAH, their disease had progressed to WHO functional class III (fatigue, chest pain and other symptoms are experienced with less than ordinary activity) with a median survival of about five years;
e) As of 2008, there remained significant gaps in knowledge about the root causes of PAH and the efficacy and safety of potential treatments;
f) Due to the complexity of the disease, PAH patients were referred to specialized PAH clinics to initiate a therapeutic plan;
g) The therapeutic plan could include supportive medications (e.g., anticoagulants or diuretics); a small percentage of patients were treated with high-dose calcium channel blockers (calcium channel blockers were not approved for PAH in Canada so this was an "off-label" use); the vast majority of patients were considered for treatment with medications developed specifically for PAH;
h) As of 2008, there were three classes of PAH medications: prostacyclin analogues, ERAs, and PDE5-Is; the approved drugs in these classes were approved for late stage patients in WHO functional classes III or IV only, partly because clinical trials focused on patients in these classes and there was a lack of understanding of long-term prognosis;
i) As of 2008, epoprostenol, a prostacyclin analogue, was considered the most effective treatment but it had to be continuously infused into the pulmonary arteries using a pump and an intravenous (IV) catheter; treprostinil was another approved prostacyclin analogue, administered by IV or subcutaneous injection; the inhaled prostacyclin analogue iloprost was approved in the U.S. and Europe but not in Canada;

j) The three known ERAs were: bosentan (approved in Canada in 2001), sitaxsentan (approved in Canada in 2007, subsequently withdrawn from the market in 2010 due to concerns about liver toxicity), and ambrisentan (approved in the U.S.); all were orally administered drugs;
k) In 2008 (and today), ERAs were only approved for PAH; their "off-label" use for other disease states was (and is) extremely limited;
l) The PDE5-I sildenafil was approved to treat PAH in 2006; tadalafil had not yet been approved for PAH but was on the market as a treatment for erectile dysfunction; prior to their approval for PAH, both sildenafil and tadalafil were sometimes used "off-label" to treat PAH; both were orally administered drugs;
m) The 2008 treatment approach was to begin with monotherapy;
n) WHO functional class III patients would typically be prescribed an ERA or PDE5-I; class IV patients would typically be prescribed epoprostenol;
o) If the initial treatment failed, the patient would stop taking that intervention and progress to the next available treatment option; combination therapy was used in limited cases as a last resort, because there was no clinical trial evidence to support this approach and the drugs were costly and not covered by provincial programs or private drug plans.

[79] Dr. McIvor's report includes a background section that describes vasoconstriction, PH and PAH, available drug treatments, and treatment approaches (monotherapy versus combination therapy). Dr. McIvor acknowledges that he did not distinguish between what was known before and after March 2008, except in a general way. Dr. McIvor's report states that the skilled person would have known the following as of 2008: information about vasoconstriction, PH and PAH, knowledge about different subtypes of PAH based on etiology, and knowledge of the WHO functional classes. As a general matter, the skilled person was aware of the categories of drugs that could be used to treat diseases of vasoconstriction and in particular, PH and PAH; however, with respect to available drug treatments and treatment approaches, the specific details about the

drugs, and strategies relating to their use, would have continued to evolve after March 6, 2008. In particular, Dr. McIvor notes that the SERAPHIN trial, a clinical trial designed to assess the effects of macitentan in patients with PAH, was completed well after March 6, 2008.

[80] Dr. McIvor did not disagree with Dr. Mielniczuk's or Dr. Kapasi's description of the CGK as of 2008.

[81] I accept that all the information described above (except the SERAPHIN trial, which was completed after 2008) was part of the skilled person's CGK as of 2008.

VI. **Claim Construction**

A. *Legal Principles*

[82] Claims are to be read in an informed and purposive way through the eyes of the skilled person: *Free World* at para 44. A purposive construction will determine whether claim elements are essential or non-essential: *Free World* at para 50; *Tearlab Corporation v I-MED Pharma Inc*, 2019 FCA 179 at paras 30-34 [*Tearlab*]. If an essential element of a claim is different or omitted, there is no infringement: *Free World* at para 31.

[83] Paragraphs 30-34 of *Tearlab* summarize key principles of claim construction:

> [30] The general principles of claim construction are now well established and were set out by the Supreme Court in three cases (*Whirlpool* at paras. 49-55; *Free World Trust v. Électro Santé Inc.*, 2000 SCC 66, [2000] 2 S.C.R. 1024 at paras. 31-67 [*Free World Trust*]; *Consolboard Inc. v. MacMillan Bloedel (Sask.) Ltd.*, 1981 CanLII 15 (SCC), [1981] 1 S.C.R. 504 at p. 520 [*Consolboard*]). These principles can be summarized as follows.

[31] The *Patent Act* promotes adherence to the language of the claims, which in turn promotes fairness and predictability (*Free World Trust* at paras. 31(a), (b) and 41). The words of the claims must, however, be read in an informed and purposive way (at para. 31(c)), with a mind willing to understand (at para. 44). On a purposive construction, it will be apparent that some elements of the claimed invention are essential while others are non-essential (at para. 31(e)). The interpretative task of the court, in claim construction, is to separate and distinguish between the essential and the non-essential elements, and to give the legal protection to which the holder of a valid patent is entitled only to the essential elements (at para. 15).

[32] To identify these elements, the claim language must be read through the eyes of a [skilled person], in light of the latter's common general knowledge (*Free World Trust* at paras. 44-45; see also *Frac Shack* at para. 60; *Whirlpool* at para. 53). As noted in *Free World Trust*:

> [51] …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 expressed 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. [Emphasis in the original.]

[33] Claim construction requires that the disclosure and the claims be looked at as a whole "to ascertain the nature of the invention and methods of its performance, … being neither benevolent nor harsh, but rather seeking a construction which is reasonable and fair to both patentee and public" (*Consolboard* at p. 520; see also *Teva Canada Ltd. v. Pfizer Canada Inc.*, 2012 SCC 60, [2012] 3 S.C.R. 625 at para. 50). Consideration can thus be given to the patent specifications to understand what was meant by the words in the claims. One must be wary, however, not to use these so as "to enlarge or contract the scope of the claim as written and … understood" (*Whirlpool* at para. 52; see also *Free World Trust* at para. 32). The Supreme Court recently emphasized that the focus of the validity analysis will be on the claims; specifications will be relevant where there is ambiguity in the claims (*AstraZeneca Canada Inc. v. Apotex Inc.*, 2017 SCC 36, [2017] 1 S.C.R. 943 at para. 31; see also *Ciba* at paras. 74-75).

> [34] Finally, it is important to stress that claim construction must be the same for the purpose of validity and for the purpose of infringement (*Whirlpool* at para. 49(b)).

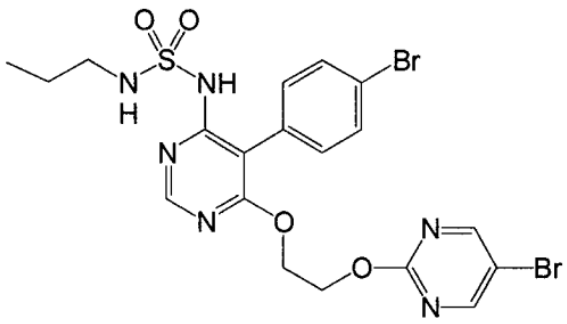
[84] As noted above, the material date for construing the claims is March 6, 2008.

[85] The parties introduced a joint claim chart outlining the plaintiffs' and defendant's proposed construction of the Asserted Claims, and it is attached as Schedule A to these Reasons. As noted above, claim construction is a question of law for the Court to decide: *Whirlpool* at para 61; *Zero Spill* at para 41.

B. *The Asserted Claims*

[86] The Asserted Claims in the 770 Patent read as follows (independent claims are in bold text):

> 1. **A product containing the compound of formula (I) below**



(I)

> **or a pharmaceutically acceptable salt of this compound, in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable salt thereof, for therapeutic use, simultaneously, separately or over a period of time, in the treatment of a disease wherein vasoconstriction is involved.**

2. A product according to claim 1, wherein the compound having PDE5-inhibitory properties is sildenafil, vardenafil, tadalafil or udenafil.

3. A product according to claim 2, wherein the compound having PDE5-inhibitory properties is tadalafil.

4. A product according to claim 2, wherein the compound having PDE5-inhibitory properties is sildenafil.

5. A product according to claim 2, wherein the disease wherein vasoconstriction is involved is hypertension, pulmonary hypertension, diabetic arteriopathy, heart failure, erectile dysfunction or angina pectoris.

…

10. A use of the compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt of said compound of formula (I), in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable sale thereof, for the manufacture of a medicament intended to treat a disease wherein vasoconstriction is involved.

11. The use according to claim 10, wherein the compound having PDE5-inhibitory properties is sildenafil, vardenafil, tadalafil or udenafil.

12. The use according to claim 11, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.

13. The use according to claim 12, wherein the compound having PDE5-inhibitory properties is sildenafil.

14. The use according to claim 12, wherein the compound having PDE5-inhibitory properties is tadalafil.

15. The use according to claim 10, wherein the disease intended to be treated is hypertension or pulmonary hypertension.

16. The use according to claim 15, wherein the disease intended to be treated is pulmonary hypertension.

17. The use according to claim 16, wherein the disease intended to be treated is pulmonary arterial hypertension.

18. The use according to claim 17, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.

19. The use according to claim 17, wherein the compound having PDE5-inhibitory properties is sildenafil.

20. The use according to claim 17, wherein the compound having PDE5-inhibitory properties is tadalafil.

21. A use of the compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt of said compound of formula (I), in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable sale thereof, for treating a disease wherein vasoconstriction is involved.

22. The use according to claim 21, wherein the compound having PDE5-inhibitory properties is sildenafil, vardenafil, tadalafil or udenafil.

23. The use according to claim 22, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.

24. The use according to claim 23, wherein the compound having PDE5-inhibitory properties is sildenafil.

25. The use according to claim 23, wherein the compound having PDE5-inhibitory properties is tadalafil.

26. The use according to claim 21, wherein the disease is selected from hypertension and pulmonary hypertension.

27. The use according to claim 26, wherein the disease is pulmonary hypertension.

28. The use according to claim 27, wherein the disease is pulmonary arterial hypertension.

29. The use according to claim 28, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.

30. The use according to claim 28, wherein the compound having PDE5-inhibitory properties is sildenafil.

31. The use according to claim 28, wherein the compound having PDE5-inhibitory properties is tadalafil.

C. *Experts' Opinions on Claim Construction*

[87] The physician experts, Dr. Mielniczuk, Dr. Kapasi, and Dr. McIvor, provided opinions on claim construction. Ms. Picard did not opine on claim construction.

[88] Dr. Mielniczuk opined that the skilled person would read claim 1 as having two main components: (i) a product containing macitentan in combination with at least one PDE5-I; (ii) for therapeutic use to treat a disease involving vasoconstriction. The skilled person would understand that the combination of macitentan and PDE5-I can be administered: (i) by the same route and at the same time; (ii) by different routes at the same time; (iii) sequentially through the same or different route of administration. Dr. Mielniczuk's report includes an appendix that summarizes the essential elements of claims 1-5 and 10-31. According to her opinion, the essential elements of claim 1 are:

> a) a product containing macitentan (or its salt);
>
> b) administered in combination with at least one PDE-5 inhibitor (or its salt);
>
> c) where (i) the product containing macitentan, and (ii) the PDE-5 inhibitor, are administered simultaneously, separately or sequentially; and
>
> d) for therapeutic use in the treatment of a disease involving vasoconstriction.

[89] Dr. Kapasi's opinion on claim 1 is similar. Dr. Kapasi's report attached an appendix that summarized the essential elements of claims 1-5 and 10-31. According to his opinion, the essential elements of claim 1 are:

> a) a product containing macitentan (or its salt);
>
> b) in combination with at least one PDE-5 inhibitor (or its salt);

> c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and
>
> d) administration of (i) the product containing macitentan and (ii) the PDE-5 inhibitor simultaneously, separately or over a period of time.

[90] Dr. McIvor opined that claim 1 covers macitentan where it is to be used in combination with a PDE5-I to treat a disease associated with the narrowing of blood vessels. The product may include both macitentan and a PDE5-I in the same dosage form, or only macitentan, provided it is used in combination with a PDE5-I to treat a disease involving vasoconstriction. Dr. McIvor opined that the skilled person would understand the reference to using macitentan in combination with a PDE5-I for therapeutic use contemplates the two drugs being used together as part of the same treatment regime to treat the same disease, which differs from the mere concomitant use of two drugs without a recognition that they would be acting in concert to treat a disease. Dr. McIvor also opined that the skilled person would refer to the definitions of "simultaneously, separately and over a period of time" in the 770 Patent disclosure, and he disagrees with Drs. Mielniczuk and Kapasi that "over a period of time" is synonymous with "one after the other". The skilled person would consider "over a period of time" to mean that the physician establishes an administration plan at the outset of treatment and this is distinguishable from the case where a second drug is started after first based on a physician's evaluation of the patient's condition, rather than a pre-defined treatment plan.

[91] The physician experts agree that claims 2-4 limit the PDE5-I to specific compounds, and claim 5 limits the diseases to hypertension, PH, diabetic arteriopathy, heart failure, erectile dysfunction, or angina pectoris.

[92] Dr. Mielniczuk opined that independent claims 10 and 21 claim the use of macitentan in combination with a PDE5-I for a particular purpose. Claim 10 is for use to manufacture a medicament for treating vasoconstrictive diseases. Claim 21 is for use in treating a vasoconstrictive disease. The skilled person would understand that the macitentan and the PDE5-I would be in dosage form for administration to the patient. According to the table appended to Dr. Mielniczuk's report, the essential elements of claim 10 are:

a) use of macitentan (or its salt);

b) for the manufacture of a medicament;

c) in combination with at least one PDE5-I (or its salt); and

d) where the medicament is intended to treat a disease involving vasoconstriction.

[93] Dr. Kapasi provides a similar opinion, and echoes that there is no limitation within claim 10 on how or when the combination is to be administered, but the 770 Patent as a whole is clear that various options are available. He summarizes the essential elements of claim 10 as follows:

a) use of macitentan (or its salt) for the manufacture of a medicament;

b) in combination with at least one PDE5-I (or its salt); and

c) where the medicament is intended to treat a disease where vasoconstriction is involved.

[94] Dr. McIvor opined that the subject matter of claim 10 is analogous to claim 1—while claim 1 refers to a product, claim 10 refers to the preparation of a medication for the same purpose. Therefore, like claim 1, claim 10 covers the use of macitentan in combination with PDE5-Is to treat diseases involving vasoconstriction.

[95] The physician experts agree that claims 11-14 are dependent on claim 10 and limit the PDE5-I to specific compounds. Claims 15-20 are also dependent on claim 10 and specify the disease being treated and/or the PDE5-I.

[96] Drs. Mielniczuk and Kapasi opine that claim 21 is for the use of macitentan in combination with a PDE5-I in treating a disease involving vasoconstriction. They state that the essential elements of claim 21 are:

a) use of macitentan (or its salt);

b) in combination with at least one PDE5-I (or its salt); and

c) for treating a disease where vasoconstriction is involved.

[97] Dr. McIvor provides the same opinion and notes that the skilled person would understand claim 21 (like claims 1 and 10) to cover the use of macitentan to treat a disease involving vasoconstriction when used in combination with a PDE5-I.

[98] Similar to the structure of claims 11-20, dependent claims 22-31 narrow the specific diseases and/or PDE5-Is.

D. *Parties' Positions on Claim Construction*

[99] According to the joint claim chart, the parties' proposed constructions for Asserted Claims appear to comprise identical essential elements. Their proposed constructions for independent claims 1, 10, and 21 are set out below.

Claim 1

a) a product containing macitentan (or its pharmaceutically acceptable salt);

b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt);

c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and

d) administration of (a) the product containing macitentan and (b) the PDE5-I, simultaneously, separately or over a period of time.

Claim 10

a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament;

b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt);

c) where the medicament is intended to treat a disease where vasoconstriction is involved.

Claim 21

a) use of macitentan (or its pharmaceutically acceptable salt);

b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt);

c) for treating a disease where vasoconstriction is involved.

[100] Despite this apparent agreement, the parties disagree on the fundamental nature of the claims, and they disagree on the purposive construction of certain claim elements.

[101] The first point of disagreement relates to the meaning of “combination”. Apotex asserts that “combination” would be understood to mean that macitentan and the PDE5-I are working in concert to treat the disease in question, and also, it would contemplate the use of macitentan and a PDE5-I where this is something a physician intended at the outset of treatment. Apotex states that simultaneously, separately, and over a period of time would receive the interpretation in the 770 Patent disclosure (at page 2), namely:

> "Simultaneously" or "simultaneous", when referring to a therapeutic use, means in the present application that the therapeutic use concerned consists in the administration of two or more active ingredients by the same route and at the same time.
>
> "Separately" or "separate", when referring to a therapeutic use, means in the present application that the therapeutic use concerned consists in the administration of two or more active ingredients at approximately the same time by at least two different routes.
>
> By therapeutic administration "over a period of time" is meant in the present application the administration of two or more ingredients at different times, and in particular an administration method according to which the entire administration of one of the active ingredients is completed before the administration of the other or others begins. In this way it is possible to administer one of the active ingredients for several months before administering the other active ingredient or ingredients. In this case, no simultaneous administration occurs.

[102] Based on these definitions, Dr. McIvor opined that "over a period of time" means the physician establishes a combination administration plan for a patient at the outset of their treatment.

[103] The plaintiffs do not dispute that "combination" would be understood to mean that macitentan and the PDE5-I are working in concert to treat the disease in question; however they disagree "combination" is limited to a combination treatment plan that is contemplated at the outset of treatment. They argue that such limitation is inconsistent with the definition of "over a period of time", which refers to two or more active ingredients administered at different times, including administration of the second ingredient several months after the first. The definition does not suggest that combination therapy is contemplated at the outset of treatment. Furthermore, limiting "combination" as Apotex suggests is inconsistent with a purposive construction in view of the CGK. As of March 2008, monotherapy was the standard of care, and

a physician typically did not establish a combination administration plan at the outset of treatment. If the initial treatment failed, another PAH medication would be considered; combination therapy was used in limited cases as a last resort. The skilled person would not interpret "combination" so as to exclude this primary method of administering two PAH therapies in 2008.

[104] Furthermore, the parties disagree on the fundamental nature of the three claim sets. Their dispute on this point affects whether, for claims 1-5, the Court is required to engage in an analysis of direct infringement or only an analysis of indirect infringement by inducement. Apotex's position is that the 770 Patent is a use patent and all of the Asserted Claims are effectively use claims, which means it would not infringe any of the Asserted Claims directly, since pharmaceutical manufacturers do not use medications. The plaintiffs state Apotex's position ignores the product and medicament elements of claims 1-5 and 10-20. They say Apotex's approach is similar to "spirit of the invention" approach that was rejected by the Supreme Court of Canada in *Whirlpool* and *Free World*. According to the plaintiffs, the Asserted Claims clearly fall into three, distinct claim sets: product claims (claims 1-5), Swiss-style use for the manufacture of a medicament claims (claims 10-20), and use claims (claims 21-31). Claims 21-31 have no product or medicament element, and they are the only claims to "just the use" of macitentan in combination with a PDE5-I to treat diseases involving vasoconstriction. While claims 1-5 and 10-20 have use elements, this does not "convert" them into use claims. With respect to claim 1, the plaintiffs state that the fourth element d) only requires that the product is *for* administration to a patient, and it does not require that administration to a patient take place. As a result, the plaintiffs assert that Apotex would infringe claims 1-5 directly, as

well as by inducing others to infringe. They allege that Apotex would also infringe claims 10-20 directly, and infringe claims 21-31 indirectly, by inducing others to infringe.

[105] The plaintiffs note that Apotex's expert witness, Dr. McIvor, does not dispute the claim construction that was put forward by Drs. Mielniczuk and Kapasi. Dr. McIvor does not dispute claim 1 to be a product claim, and he describes claim 10 as being related to the use of macitentan not merely as a treatment, but rather, for the manufacture of a medicament.

[106] Apotex states the experts recognized that the subject matter of claims 21-31 is largely indistinguishable from the subject matter of claims 1-5 and 10-20, and none of the experts suggest that the 770 Patent is focused on a new product, new medicament, or new formulation. Notwithstanding the reference to a "product" in claim 1 (and in dependent claims 2-5), the expert witnesses agreed that an essential element of these claims is the use of macitentan in combination with a PDE5-I and its administration to a patient (whether separately, sequentially, or over a period of time). Similarly, though claim 10 states "the manufacture of a medicament", claims 10-20 are fundamentally "use claims" directed at the use of macitentan in combination with a PDE5-I and how it is administered to patients.

[107] Apotex submits the plaintiffs' approach seeks to have the Court redraft the claims, and ignores that all of the Asserted Claims are fundamentally directed at the use of macitentan as a combination therapy. The plaintiffs' approach is without foundation, as the law is clear that the claims of a patent are tethered to what has purportedly been invented: *Patent Act*, s 27(4). A claim is not an "added description of the invention, but a limitation of the description of the

invention contained in the body of the specification": *Merck & Co Inc v Pharmascience Inc*, 2010 FC 510 at para 44.

[108] According to Apotex, a purposive claim construction orients the analysis at what has actually been invented. This logic was applied in *Hoffman-La Roche Limited v Sandoz Canada Inc*, 2021 FC 384 (at paragraphs 97-98) [*Hoffman-La Roche*] to reject the patentee's attempt to enlarge the scope of "use" claims by recasting them as product claims. In *Hoffman-La Roche*, Justice Manson rejected an argument that the asserted claims could be categorized into three distinct claim forms (German-style claims, Swiss-style claims, and "product for use"-style claims) as being an argument of form over substance:

> [97] Roche's approach seeks a finding of claim *form* over *substance*. In doing so, it obscures the proper approach to claims construction. As discussed above, the claims construction exercise emphasizes a purposive construction. In this case, the 654 and 997 Asserted Claims have been properly construed as use claims, as provided above. […] The alleged invention in this case resides in the use of pirfenidone, whether in the context of the 654 or 997 Patent, and not in the manufacture or composition of pirfenidone, a known compound.
>
> [Emphasis in original.]

[109] According to Apotex, all of the physician experts opined that the use of macitentan to treat certain diseases is an essential element of the claims, and there is no reason for this Court—either as a matter of law or based on expert opinion—to rewrite the claims of the 770 Patent and thereby engage in an analysis of direct infringement.

E. *Analysis on Claim Construction*

[110] On the first point of the parties' disagreement, I find that claim 1 is not limited to the use of macitentan with a PDE5-I that is contemplated by the physician at the outset of treatment.

[111] The 770 Patent specification does not indicate that any of the alternatives for therapeutic administration are tied to the timing of a prescribing physician's decision. The definitions of "simultaneously, separately or over a period of time" in the 770 Patent specification reflect a broad range of ways that the two or more active ingredients could be administered in combination. They are not limited to simultaneous administration, and could be administered at the same time via the same route, separately via different routes, or one after the other.

[112] The skilled person would construe the claim in light of the CGK, including that: (i) ERAs were only approved for PAH; (ii) monotherapy was the standard of care for PAH in 2008; (iii) combination therapy was used in limited cases as a last resort, when treatment with a single medication failed. Dr. Mielniczuk opined that physicians took a deterioration approach to PAH, only escalating therapy once the patient's condition had worsened. Dr. McIvor's testimony in cross-examination was that monotherapy was the standard of care for PAH in 2008, and the most likely situation for combination treatment at that time would be an approach of giving a patient a drug, monitoring how they were doing, and if they did not improve, either move the patient to a different drug (sequential monotherapy) or add a second drug (combination therapy). He agreed that this would fall within the meaning of "combination" in the 770 Patent.

[113] For these reasons, I find that the skilled person would not read claim 1 so as to exclude what the skilled person would have considered to be a likely way that the claimed combination would be administered to PAH patients in 2008.

[114] I will now turn to the parties' dispute regarding the fundamental nature of the three claim sets of the Asserted Claims. For ease of reference, I have reproduced the language of each independent claim and the essential elements as proposed by the parties in the joint claim chart.

(a) *Claims 1-5*

Claim 1	**Parties' proposed construction**
1. A product containing the compound of formula (I) below or a pharmaceutically acceptable salt of this compound, in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable salt thereof, for therapeutic use, simultaneously, separately or over a period of time, in the treatment of a disease wherein vasoconstriction is involved	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt); c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and d) administration of (a) the product containing macitentan and (b) the PDE5-I, simultaneously, separately or over a period of time.

[115] With respect to claim element d), the plaintiffs state that the Court must determine whether the element requires that administration to a patient take place, or solely that the product be *for* that administration. According to the plaintiffs, if the Court determines that element d) requires only that the product be *for* that administration, Apotex would infringe claim 1 directly.

[116] It is apparent that the word “administration” does not appear in claim 1, and the physician experts do not fully explain why they considered administration of the combination to be a separate, essential element. The 770 Patent specification defines simultaneously, separately or over a period of time as ways to administer the combination. However, a plain reading of claim 1 ties “simultaneously, separately, or over a period of time” to “for therapeutic use”, while the parties’ proposed construction breaks that connection by identifying administration as a separate essential element.

[117] The focus of purposive claim construction is on the language of the claims, which define the monopoly: *Patent Act*, s 27(4). The disclosure should not be used to enlarge or contract the scope of the claims as written and understood: *Tearlab* at para 33, citing *Whirlpool* at para 52 and *Free World* at para 32. When the words of claim 1 are read in the order that they appear, the elements would be:

a) a product containing macitentan (or its pharmaceutically acceptable salt);

b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt);

c) for therapeutic use, simultaneously, separately or over a period of time, in the treatment of a disease wherein vasoconstriction is involved.

[118] A plain reading of claim 1 does not suggest that administration to a patient is an essential element. I find that the skilled person would not consider administration to a patient to be an essential element.

[119] I agree with the parties and their experts that "in combination" is an essential element. I also agree with the parties and their experts that the claim language does not tie the element of "in combination" to the product that contains macitentan (the first essential element). Dr. McIvor opined that claim 1 covers a product that includes both macitentan and a PDE5-I, or a product that includes only macitentan provided it is used in combination with a PDE5-I. It necessarily follows that, in his opinion, the product of claim 1 is not limited to a product that contains both macitentan and a PDE5-I. Although the plaintiffs' experts did not expressly address whether claim 1 covers a product that contains macitentan and a PDE5-I, they opined that it covers a product that includes only macitentan provided it is used in combination with a PDE5-I. Therefore, like Dr. McIvor, they did not tie "in combination" to the product.

[120] In my view, the skilled person would read claim 1 to cover an embodiment where two active ingredients—macitentan and a PDE5-I—are combined either in the same dosage form or in a package that has two dosage forms, but would not read claim 1 to be limited to such embodiment. Claim 1 also covers a product that only contains macitentan, provided that the other claim elements are satisfied. Where a product does not contain macitentan in combination with a PDE5-I, there must be a combination of the product and a PDE5-I.

[121] The plain reading is consistent with the disclosure. The first paragraph of the 770 Patent, describing what the invention relates to, is a verbatim recitation of claim 1. In my view, claim 1 would therefore be a broad claim.

[122] I find the elements of claim 1 are:

Claim 1

a) a product containing macitentan (or its pharmaceutically acceptable salt);

b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt);

c) for therapeutic use, simultaneously, separately or over a period of time, in the treatment of a disease wherein vasoconstriction is involved.

[123] Claim elements are presumed to be essential: *Mediatube Corp v Bell Canada*, 2017 FC 6 at para 33. On a purposive construction, I find that they are all essential elements.

[124] The limitations that are added by the dependent claims 2-4 are straightforward and non-controversial. On a purposive construction, claims 2-5 add the following limitations:

Claim 2: the PDE5-I is sildenafil, vardenafil, tadalafil or udenafil.

Claim 3: the PDE5-I is tadalafil.

Claim 4: the PDE5-I is sildenafil.

Claim 5: the disease wherein vasoconstriction is involved is hypertension, pulmonary hypertension, diabetic arteriopathy, heart failure, erectile dysfunction or angina pectoris.

(b) *Claims 10-20*

Claim 10	**Parties' proposed construction**
10. A use of the compound of formula (I) as defined in claim 1, or a pharmaceutically acceptable salt of said compound of formula (I), in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable salt thereof, for the manufacture of a	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt);

medicament intended to treat a disease wherein vasoconstriction is involved.	c) where the medicament is intended to treat a disease where vasoconstriction is involved.

[125] As seen from the comparison, the parties' proposed construction changes the order of the words in claim 10. Claim 10 reads (omitting the pharmaceutically acceptable salt for simplicity): a use of macitentan, in combination with at least one PDE5-I, for the manufacture of a medicament intended to treat a disease wherein vasoconstriction is involved. The proposed construction of claim 10 is: a use of macitentan, for the manufacture of a medicament intended to treat a disease wherein vasoconstriction is involved, in combination with at least one PDE5-I.

[126] Claim 10 is what is known as a "Swiss-style" claim, a recognized claim structure. As Justice Manson noted in *Hoffman-La Roche*, Swiss-style claims are not invariably construed in the same way and they do not "automatically benefit from a literal construction": *Hoffman-La Roche* at para 102. Recognizing the context-specific claims construction exercise, Justice Manson stated "Swiss-style claims may be construed as use claims where the circumstances warrant." Justice Manson found that such a construction was warranted in that case. He held that the Swiss-style structure of the claims at issue in that case could not be used to "claim a novel product for use in a medicament when in fact that product used in a medicament is no longer novel": *Hoffman-La Roche* at para 102.

[127] The plaintiffs argue that a purposive claim construction recognizes that a Swiss-style claim is a type of product claim. According to the plaintiffs, claim 10 has both a product element (a medicament) and a use element in that the medicament is used for treatment in combination with a PDE5-I. Apotex argues that a purposive claim construction orients the analysis at what

was invented. Claims 10-20 are fundamentally oriented at the use of macitentan, and in particular, how it is administered to patients. Apotex states this logic was applied in *Hoffman-La Roche* to reject the patentee's attempt to enlarge the scope of use claims by recasting them as product claims. The plaintiffs counter that Apotex's construction ignores the medicament element of 10.

[128] As noted above, a purposive construction focuses on the language of the claims. The words chosen by the patentee necessarily play a key role: *ABB Technology AG v Hyundai Heavy Industries Co, Ltd*, 2015 FCA 181 at paras 42-43. In my view, the parties' proposed construction strains the language of claim 10, rearranging the words of the claim to enlarge its scope. On a plain reading, claim 10 relates to a use for the manufacture of a medicament, and claim 10 ties "in combination" to that use. In other words, claim 10 claims the use of the combination—macitentan and a PDE5-I—for the manufacture of a medicament.

[129] Apotex's concern, that the Swiss-style structure of claims 10-20 should not be used to claim a novel product for use in a medicament when the product is not novel, does not apply. This case does not raise the same concern as in *Hoffman-La Roche*, because claim 10 includes the element "in combination", and the 770 Patent relates to a novel combination involving macitentan and a PDE5-I.

[130] I find the elements of claim 10, which are all essential elements, to be:

Claim 10

a) use of macitentan (or its pharmaceutically acceptable salt);

b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt);

c) for the manufacture of a medicament intended to treat a disease wherein vasoconstriction is involved.

[131] The limitations that are added by dependent claims 11-20 are straightforward and not controversial. On a purposive construction, claims 11-20 add the following limitations:

Claim 11: the PDE5-I is sildenafil, vardenafil, tadalafil or udenafil.

Claim 12: the PDE5-I is sildenafil or tadalafil.

Claim 13: the PDE5-I is sildenafil.

Claim 14: the PDE5-I is tadalafil.

Claim 15: the disease is hypertension or PH.

Claim 16: the disease is PH.

Claim 17: the disease is PAH.

Claim 18: the disease is PAH and the PDE5-I is sildenafil or tadalafil.

Claim 19: the disease is PAH and the PDE5-I is sildenafil.

Claim 20: the disease is PAH and the PDE5-I is tadalafil.

(c) *Claims 21-31*

Claim 21	**Parties' proposed construction**
21. A use of the compound of formula (I) as defined in claim I, or a pharmaceutically acceptable salt of said compound of formula (I), in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable salt thereof for treating a disease wherein vasoconstriction is involved.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE5-I (or its pharmaceutically acceptable salt); c) for treating a disease where vasoconstriction is involved.

[132] I agree with the parties and the physician experts that claim 21, purposively construed, has the following essential elements:

> *Claim 21*
>
> a) use of macitentan (or its pharmaceutically acceptable salt);
>
> b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt);
>
> c) for treating a disease where vasoconstriction is involved.

[133] On a purposive construction, claims 22-31 mirror the limitations of claims 11-20:

> *Claim 22*: the PDE5-I is sildenafil, vardenafil, tadalafil or udenafil.
>
> *Claim 23*: the PDE5-I is sildenafil or tadalafil.
>
> *Claim 24*: the PDE5-I is sildenafil.
>
> *Claim 25*: the PDE5-I is tadalafil.
>
> *Claim 26*: the disease is hypertension or PH.
>
> *Claim 27*: the disease is PH.
>
> *Claim 28*: the disease is PAH.
>
> *Claim 29*: the disease is PAH and the PDE5-I is sildenafil or tadalafil.
>
> *Claim 30*: the disease is PAH and the PDE5-I is sildenafil.
>
> *Claim 31*: the disease is PAH and the PDE5-I is tadalafil.

VII. **Infringement**

[134] The *Patent Act* grants to a patentee the exclusive right, privilege and liberty of making, constructing and using the invention and selling it to others to be used: *Patent Act*, s 42; *Monsanto Canada Inc v Schmeiser*, 2004 SCC 34 at para 25 [*Monsanto*]. Infringement is an act

that deprives the inventor in whole or in part, directly or indirectly, of full enjoyment of the monopoly conferred by law: *Monsanto* at para 35.

[135] In proceedings under the *PMNOC Regulations*, infringement relates to the actions of the "second person": *Aventis Pharma Inc v Pharmascience Inc*, 2006 FCA 229 at paras 55-59.

[136] The plaintiffs bear the burden of proving infringement: *Monsanto* at para 29.

A. *Direct Infringement*

(1) Parties' Submissions

[137] The plaintiffs allege that Apotex will directly infringe claims 1-5 and 10-20 of the 770 Patent. They allege Apotex is not seeking approval for a "non-patented" use—macitentan has one approved indication and one use in practice, which is to treat patients with PAH. Combination treatment is the standard of care for PAH patients in Canada, and most patients who are prescribed macitentan will also receive a PDE5-I.

[138] The plaintiffs state that claims 1-5 of the 770 Patent are product claims, and a product claim can be infringed by a product that is adapted for a patented use: *Janssen Inc v Teva Canada Limited*, 2020 FC 593 at paras 35, 252-256 [*Teva Paliperidone*]; *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2018 FC 259 at paras 298-300, 303, 318, aff'd on this issue 2020 FCA 30 at para 41. They allege claims 1-5 of the 770 Patent would be infringed by a product that contains macitentan if the product is for use in combination with a

PDE5-I. Therefore, Apotex will directly infringe claims 1-5 by making and selling APO-MACITENTAN, for use in combination with a PDE5-I for the treatment of PAH.

[139] Similarly, the plaintiffs state that Apotex will infringe claims 10-20 directly, because macitentan will be used in the manufacture of APO-MACITENTAN, and APO-MACITENTAN will be for use in combination with a PDE5-I to treat PAH.

[140] Apotex alleges the plaintiffs' approach ignores that claims 1-5 and 10-20 are directed at the use of macitentan in combination with PDE5-I to treat certain diseases. If use is an essential element of a claim, there can be no direct infringement where the alleged infringer does not use the drug for the claimed purpose: *Hoffman-La Roche* at para 109. Apotex states there is no basis to find that it will infringe any of the Asserted Claims directly, because it would not administer macitentan to patients.

(2) Analysis

[141] Drs. Mielniczuk and Kapasi compared the essential elements of the Asserted Claims to how APO-MACITENTAN will be used, if it is approved. For claim 1, they opined that the essential elements will be present as follows: a) APO-MACITENTAN will contain macitentan; b) it will be administered in combination with a PDE5-I (or its salt), particularly sildenafil citrate or tadalafil; c) it will be for therapeutic use in the treatment of a disease where vasoconstriction is involved, specifically PAH; and d) APO-MACITENTAN and the PDE5-I will be administered simultaneously, separately or over a period of time/sequentially. For claim 10, they opined that the essential elements will be present as follows: a) Apotex will use macitentan for the

manufacture of a medicament, namely APO-MACITENTAN; b) APO-MACITENTAN will be used in combination with a PDE5-I (or its salt), in particular sildenafil citrate or tadalafil; and c) APO-MACITENTAN will be intended to treat a disease where vasoconstriction is involved, in particular PAH.

[142] Dr. Mielniczuk's and Dr. Kapasi's evidence was that claim 1 and claim 10 include an element of administration of a product containing macitentan and a PDE5-I to a patient. They acknowledged on cross-examination that a drug company does not administer drugs to patients, which is something that a physician or patient would do.

[143] Dr. McIvor opined that there will be no direct infringement because, among other things, each of the Asserted Claims has a common underlying element of the use of macitentan in combination with a PDE5-I. Dr. McIvor opined that Apotex will not use APO-MACITENTAN in combination with a PDE5-I to treat a disease involving vasoconstriction, including PAH.

[144] For the reasons set out in the claim construction section, I have found that claim sets 1-5 and 10-20 do not include an essential element of administration to a patient. However, it is an essential element of these claims that macitentan be "in combination" with at least one PDE5-I, and not, as the plaintiffs assert, that the product containing macitentan (claims 1-5) or medicament containing macitentan (claims 10-20) simply be "for use in combination" with a PDE5-I. The evidence did not establish that Apotex will: (i) make, use or sell a product that contains macitentan in combination with a PDE5-I; (ii) combine a product that contains macitentan with a PDE5-I to treat PAH; or (iii) use macitentan in combination with a PDE5-I to

manufacture a medicament. Apotex will not infringe these claims directly as it does not perform the “in combination” element.

[145] I would reach the same conclusion on direct infringement based on the proposed construction put forward by the parties. In addition to the combination element, their proposed construction includes an essential element of administration. All of the physician experts agreed that Apotex does not administer macitentan and PDE5-Is to patients.

[146] In conclusion, Apotex will not infringe claims 1-5 and 10-20 directly.

B. *Inducing Infringement*

[147] A generic drug manufacturer may be implicated in the infringement by others if it induces that infringement. The three-prong test for inducing infringement is set out in *Corlac Inc v Weatherford Canada Ltd*, 2011 FCA 228 at paragraph 162 [*Corlac*], leave to appeal to SCC refused 34459 (29 March 2012):

1. The acts of infringement must have been completed by the direct infringer;
2. The completion of the acts of infringement must be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place; and
3. The influence must be knowingly exercised by the inducer; in other words, the inducer knows that this influence will result in the completion of the acts of infringement.

(1) Parties' Submissions

[148] The plaintiffs submit the test for infringement is expansive, capturing any activity that deprives the patentee of their full use of the invention: *Monsanto* at paras 35-37. Inducement is a form of infringement.

[149] The plaintiffs argue that infringement is a question of fact and the outcomes of various inducing infringement cases in the pharmaceutical context turn on the evidence. Generic manufacturers have been successful where the evidence showed that direct infringement under prong 1 of the test was unlikely or the generic PM did not refer to or suggest the infringing use under prong 2 (i.e. the generic PM was a "skinny label"). Patentees have been successful where the evidence showed direct infringement would happen and the generic manufacturer was implicated, often because, despite the generic manufacturer's claims to the contrary, the PM was not "skinny".

[150] The plaintiffs argue that the first prong of the *Corlac* test is met—there will be direct infringement of claims 1-5 and 21-31 of the 770 Patent by physicians and patients. If approved, APO-MACITENTAN will be used for the treatment of PAH in combination with a PDE5-I, most commonly tadalafil.

[151] The plaintiffs submit the crux of the dispute relates to the second prong. In this regard, the generic manufacturer's PM plays a key role in determining inducement: *AB Hassle v Canada (Minister of National Health and Welfare)*, 2002 FCA 421 at para 55 [*AB Hassle*]. The APO-

MACITENTAN PM will induce physicians to prescribe APO-MACITENTAN in combination with a PDE5-I to treat PAH.

[152] The plaintiffs state this is not a "skinny label" case. Apotex seeks approval for a single indicated use, and it is the same use indicated for OPSUMIT: the treatment of WHO functional class II or III (intermediate risk) PAH patients. Macitentan is not approved for any other use, and nothing in the APO-MACITENTAN PM communicates to physicians that it should be used any differently than OPSUMIT.

[153] The product monograph is to be considered as a whole: *Janssen Inc v Apotex Inc*, 2021 FC 7 at para 242. The APO-MACITENTAN PM includes bioequivalence data and results from SERAPHIN, which is the trial that established macitentan is safe and effective as a monotherapy and in combination with a PDE5-I. At enrollment, 61% of the patients in SERAPHIN were receiving a PDE5-I. In addition, the drug interaction section of the APO-MACITENTAN PM states that [redacted]. The inclusion of the SERAPHIN results along with the bioequivalence information will inform physicians that APO-MACITENTAN is safe and effective for use in combination with a PDE5-I, and encourage physicians to use APO-MACITENTAN just as OPSUMIT is used—in combination with PDE5-Is. Drs. Mielniczuk and Kapasi opined that physicians will review the information in the APO-MACITENTAN PM and rely on that information in the course of prescribing APO-MACITENTAN.

[154] The plaintiffs submit Dr. Mielniczuk's and Dr. Kapasi's evidence should be preferred over that of Apotex's expert witnesses. Drs. Mielniczuk and Kapasi regularly prescribe PAH medications and recently participated in the creation of Canadian consensus guidelines, working with other PAH experts and gaining an understanding of their practices. Ms. Picard's evidence should be given no weight because she cannot speak to the key issue of whether the PM would influence a prescribing physician. Although Dr. McIvor was qualified as a respirologist, he is not an expert in PAH and he does not regularly prescribe PAH medications. His first-hand experience with PAH comes from interactions with in-patients with undifferentiated diagnosis at the hospital. When these patients are diagnosed with PAH, they are referred to Dr. McIvor's colleagues who actually specialize in the area. Dr. McIvor conceded that the process in his report of reviewing, as part of his mandate, blacklined PMs or side-by-side comparisons of the brand and generic PMs for macitentan were an artificial exercise. Furthermore, he holds a general view that PMs do not influence prescribers and his opinions would not change regardless of what the APO-MACITENTAN PM says. The plaintiffs argue that Dr. McIvor's evidence about the contents of the APO-MACITENTAN PM is not of assistance to the Court due to both a lack of experience in PAH and a fundamental disregard for the documents he was opining on, and his opinion should be given no weight.

[155] The plaintiffs submit this case is analogous to *AB Hassle v Genpharm Inc*, 2004 FCA 413 [*Genpharm*] and *Abbott Laboratories Limited v Canada (Minister of Health)*, 2006 FC 1411, aff'd 2007 FCA 251 [*Novopharm*]. In *Genpharm*, the Federal Court of Appeal affirmed the trial court's finding of inducement, where the trial court held that the inclusion of studies referring to the patented use amounted to "blatant attempts" to leave the reader of the PM with the

impression that the generic product may be used for the patented use. In *Novopharm*, a similar ruling was upheld on a similar basis.

[156] Accordingly, Apotex's activities will be the "but-for" cause of infringement. This remains the case even if a physician applies their own skill and judgment to the decision to prescribe combination therapy. If it were otherwise, inducing infringement could never be found in the context of pharmaceutical patents: *Janssen Inc v Pharmascience Inc*, 2022 FC 62 at paras 132-133, 137 [*Pharmascience Paliperidone*]; *Janssen Inc v Apotex Inc*, 2022 FC 107 at paras 142-143, 148 [*Apotex Paliperidone*]. Furthermore, a "but for" test does not mean that Apotex's activities must be the sole cause of the infringement: *Athey v Leonati* (1996), [1996] 3 SCR 458, 140 DLR (4th) 235.

[157] With respect to prong 3 of the *Corlac* test, the plaintiffs argue that this element is not difficult to meet. Knowledge can be inferred where the inducer created and distributed the source of the influence: *Apotex Paliperidone* at paras 149-150; *Western Oilfield Equipment Rentals Ltd v M-I LLC*, 2019 FC 1606 at para 133; *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2020 FCA 30 at para 44 [*Hospira FCA*]. Apotex is in control of its APO-MACITENTAN product and the contents of its PM, which will be made available to physicians, and at least some physicians will be influenced to infringe. Apotex is or ought to be aware that it will exercise influence on how its product will be used.

[158] Apotex states that the test for inducement is stringent, and a difficult test to meet. Apotex argues the plaintiffs are seeking to have this Court grant a *de facto* monopoly over the use of

macitentan as a monotherapy. This would result in a real injustice, as it would artificially extend the plaintiffs' monopoly over macitentan: *AB Hassle* at para 57.

[159] Apotex states the plaintiffs understate the law by arguing that each case turns on its evidence—the prior jurisprudence is instructive to inform the analysis.

[160] With respect to the first element, while Apotex acknowledges the clear possibility of "off-label" use of macitentan in combination with a PDE5-I, Apotex submits that the plaintiffs have failed to meet their burden. The evidence does not establish that a physician will write a prescription for APO-MACITENTAN in combination with a PDE5-I, or write a prescription for OPSUMIT or macitentan in combination with a PDE5-I, which will be filled with APO-MACITENTAN by the pharmacy.

[161] Like the plaintiffs, Apotex argues that the core of this case comes down to influence. Apotex's main arguments relate to the second prong of the *Corlac* test.

[162] Apotex asserts that it is not seeking approval for the use enumerated in the Asserted Claims and the APO-MACITENTAN PM does not encourage physicians to prescribe APO-MACITENTAN for that use. Apotex notes that there remains a role for monotherapy in the treatment of PAH for a non-trivial number of patients, approximately 10-30% depending on which data set is considered.

[163] Apotex submits an inducement to infringe generally cannot be inferred from a mere reference to the claimed use in a PM, for example, in the course of explaining contraindications or drug interactions, or as part of a list of scientific references: *Novopharm Limited v Sanofi-Aventis Canada Inc*, 2007 FCA 167 at paras 10-11. Apotex emphasizes that the analysis should be focused on what the PM instructs, instead of how a product may ultimately be used by the physician: *Bayer Inc v Pharmaceutical Partners of Canada Inc*, 2015 FC 797 at paras 59-61, 64 [*Bayer*], aff'd 2016 FCA 13.

[164] Apotex argues the APO-MACITENTAN PM does not teach that APO-MACITENTAN can be used in combination with a PDE5-I. The "Indications and Clinical Use" section does not suggest that APO-MACITENTAN can be used with a PDE5-I and any such use would be "off-label". References to [redacted], and the mention of SERAPHIN, are precisely the type of stray and subtle references that the Courts have held not to give rise to inducement. The APO-MACITENTAN PM removed all mentions to the use of macitentan as a combination therapy that are present in the OPSUMIT PM, and only mentions SERAPHIN results that reported macitentan was useful as a monotherapy. The PM does not provide directions on how to administer APO-MACITENTAN in combination with a PDE5-I, including whether it should be administered simultaneously, separately, or over a period of time.

[165] Apotex submits this case is indistinguishable from *Lundbeck Canada Inc v Ratiopharm Inc*, 2009 FC 1102 [*Lundbeck*], where the patent claimed the use of a drug as part of a combination but Ratiopharm's PM only taught the use of the drug as a monotherapy. In

addition, Ratiopharm was not seeking approval for use of the drug in combination with any other drugs.

[166] Apotex submits the notion of "but for" causation in the second prong of the test requires proof that the defendant's wrongful conduct is the necessary cause of the direct infringement, and without the influence, the direct infringement would not have occurred: *Ediger v Johnston*, 2013 SCC 18 at para 28. Apotex states it is insufficient to establish that a defendant is partially responsible for the infringement, and argues that *Bayer Inc v Pharmaceutical Partners of Canada Inc*, 2015 FC 388 at paragraph 26 (aff'd 2015 FC 797 and 2016 FCA 13) and *Apotex Inc v Nycomed Canada Inc*, 2011 FC 1441 at paragraphs 19-21, 27-28, support this proposition. Apotex submits that APO-MACITENTAN PM cannot be the "but for" cause when PAH specialists base their prescribing decisions on clinical studies and their practice experience. In the field of PAH, the physicians know SERAPHIN very well and it does not matter what is contained in APO-MACITENTAN PM. Apotex argues that prescription decisions, including how and when to use macitentan as part of a combination treatment, would not be informed by what is set out in the APO-MACITENTAN PM in any material way.

[167] With respect to the third prong of the *Corlac* test, Apotex notes that the knowledge at issue is the knowledge that influence is being exercised, and not knowledge that the resulting activity will infringe: *Hospira FCA* at para 45. Apotex submits there is no evidence to establish it has such knowledge. To the contrary, the evidence shows that Apotex has "scrubbed clean" its PM of any mention of combination use of macitentan with PDE5-I.

(2) Analysis

(a) *Corlac Test: Prong 1*

[168] The first prong of the *Corlac* test requires an act of infringement that must have been completed by the direct infringer: *Corlac* at para 162. There is no requirement for direct contact between the inducer and the direct infringer, and the alleged inducer need not supply all components or elements of the claimed invention: *Apotex Paliperidone* at para 116.

[169] While Apotex argued in its closing submissions that the evidence did not establish direct infringement by a physician, Apotex did not "press this point too hard" because it acknowledged the clear possibility of "off-label" use. Dr. McIvor acknowledged that physicians might prescribe APO-MACITENTAN for use in combination with a PDE5-I; however, he opined that this would be an "off-label" use.

[170] Dr. Mielniczuk opined that if Apotex is permitted to sell APO-MACITENTAN with the proposed APO-MACITENTAN PM, the "on-label" use will be the same as OPSUMIT. She opined that every patient who receives APO-MACITENTAN will be a patient that would have otherwise received OPSUMIT for PAH and that in most instances, the use will be in combination with a PDE5-I. In her opinion, the vast majority (approximately 80%) of the use of APO-MACITENTAN will be to treat PAH in combination with a PDE5-I.

[171] Dr. Kapasi opined that physicians will use APO-MACITENTAN in the same way OPSUMIT is used to treat patients with PAH. In most cases (about 80-90% of the time), APO-MACITENTAN will be prescribed in combination with another PAH-specific treatment, which

most frequently will be a PDE5-I (about 80% of the time), most often tadalafil. Dr. Kapasi stated that practically speaking, there is no use for OPSUMIT or APO-MACITENTAN other than in treating patients with PAH, and as with OPSUMIT, if APO-MACITENTAN is approved, he expects there will be little, if any, "off-label" use.

[172] Dr. McIvor opined that a physician who reads the APO-MACITENTAN PM will be alerted to the fact that Apotex only intends its product to be used as a monotherapy. As such, if a physician intends to prescribe macitentan for use as part of a combination therapy, it is his view that they would likely prescribe OPSUMIT rather than APO-MACITENTAN. However, Dr. McIvor also opined that in his experience, physicians do not generally consult PMs when prescribing a given drug, and that a physician will tend to do what is best for his or her patients, even if it contradicts the intentions or hopes of a pharmaceutical company.

[173] In the context of his opinion on inducing infringement, Dr. McIvor stated that APO-MACITENTAN may be prescribed for use in combination with PDE5-Is or other products where OPSUMIT is unavailable, where cost considerations militate in favour of ensuring the generic product is used, or where a patient is expected to better tolerate the excipients in the generic product. In these cases, physicians will either recognize that this use is "off-label" the APO-MACITENTAN PM or, indeed, may be unaware of what the APO-MACITENTAN PM sets out. In either case, the decision will be taken by the physician without the influence of Apotex.

[174] On cross-examination, Dr. McIvor agreed that combination therapy is the standard of care for most PAH patients. He also testified:

> Q. Apo-macitentan isn't going to be prescribed by doctors or used by patients for diseases other than PAH to your expectation, fair?
>
> A. Yes, that's correct.
>
> Q. So not going to be prescribed or used for a disease for which it is not indicated, correct?
>
> A. That's right. I[t] will be used as prescribed by the physician for what they presume to be something that would benefit the patient, PAH.
>
> Q. Right. I think you would agree, and perhaps already have agreed, that perhaps some of those patients will also be prescribed a PDE5 inhibitor for their PAH, correct?
>
> A. Some people with PAH, yes, will already be [on] a PDE5 inhibitor, yes.

[175] The evidence establishes that, if approved, APO-MACITENTAN will be combined with a PDE5-I (sildenafil, or more commonly, tadalafil) for the treatment of PAH. The plaintiffs have established that prescribing physicians and patients will directly infringe claims 1-5 and 21-31.

(b) *Corlac Test: Prong 2*

[176] Under the second prong of the *Corlac* test, the completion of the acts of infringement must be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place: *Corlac* at para 162. This has sometimes been described as a "but for" test.

[177] In the context of pharmaceutical patent litigation, inducement requires more than the mere sale of a generic drug, or a recognition that the generic drug will likely be used to infringe a patent: *AB Hassle FCA* at para 57; *Aventis Pharma Inc v Apotex Inc*, 2005 FC 1461 at para 32,

aff'd 2006 FCA 357; *Solvay Pharma Inc v Apotex Inc*, 2008 FC 308 at para 136; *Bristol-Myers Squibb Canada v Apotex Inc*, 2017 FC 1061 at para 37.

[178] As noted above, Apotex states the plaintiffs' position that each case turns on its own evidence does not give due consideration to the prior jurisprudence. Apotex points to cases where bioequivalence data, references to clinical trial results, and the mention of a patented use in a PM, for example in the context of drug interaction safety information, were insufficient to satisfy the second prong of the inducement test, and argues that those cases should inform the analysis in this case.

[179] While I agree with Apotex that prior jurisprudence is instructive to inform an inducement analysis, the *Corlac* test requires an application of factual findings to the legal test. Each case will turn on the totality of the evidence that is before the Court, and prior jurisprudence does not override the evidence-driven exercise that must be undertaken. In three recent decisions of this Court involving the same drug (paliperidone), differences in the evidence led to different findings on inducement: *Teva Paliperidone*; *Pharmascience Paliperidone*; *Apotex Paliperidone*.

[180] I note as well that many cases cited by Apotex were decided in a different context, under the former *PMNOC Regulations*. As Justice Manson noted in *Teva Paliperidone* at paragraph 257:

> In applications under the old Patented Medicines (Notice of Compliance) regime, the relevant inquiry was whether allegations of non-infringement were justified. Pursuant to the September 2017 amendments, proceedings under the *Regulations* are full patent actions. In inducement cases under the pre-September 2017 regime, the Court noted that should the generic come to market and

> begin inducing infringement, the brand owner would still have recourse to an action for infringement (see, for example, *Bayer Inc v Pharmaceutical Partners of Canada Inc*, 2015 FC 388 at para 33; *Lundbeck Canada Inc v Ratiopharm Inc*, 2009 FC 1102 at para 383 [*Lundbeck*]). This is no longer the case under the new regime.

[181] I agree with the plaintiffs that, even if a physician applies their own skill and judgment to the decision to prescribe combination therapy, this is not inconsistent with the "but for" test. The degree of influence required to satisfy the second prong of the *Corlac* test may vary from case to case, and it will depend on the evidence.

[182] In this case, the evidence for the prong 2 exercise relates to how physicians who prescribe PAH drugs would understand the content of the APO-MACITENTAN PM and whether it would influence such physicians to prescribe APO-MACITENTAN in combination with a PDE5-I.

[183] The physician experts agree that the current standard of care for PAH patients is combination treatment, and most commonly, the combination is an ERA and PDE5-I. In this regard, Dr. Mielniczuk opined that the vast majority of the use of APO-MACITENTAN will be to treat PAH in combination with a PDE5-I. Similarly, Dr. Kapasi opined that in most cases, APO-MACITENTAN will be prescribed in combination with another PAH-specific treatment, which most frequently will be a PDE5-I, and most often tadalafil. In their reports, Drs. Kapasi and Mielniczuk estimated the percentage of patients receiving combination therapy with macitentan and a PDE5-I to be about 80% or more, without providing a basis for this estimate. When questioned in cross-examination, they explained that the estimates were based on OPSUMIT data from a PAH advisory board for Janssen and their own clinical practices. It was clear that these were rough estimates based on partial data, and certain market data estimates

showed that approximately 30% of patients who were receiving OPSUMIT were receiving it as monotherapy. In summary, while these were rough estimates, I am satisfied that more than a majority of PAH patients who are prescribed OPSUMIT also receive a PDE5-I in combination.

[184] PAH is a rare disease, affecting around 25-30 people per million. The prescription of PAH drugs is controlled in Canada—in most provinces, macitentan can only be prescribed by a limited number of specialist physicians who work in recognized PH centres. Dr. Kapasi stated that across Canada, there are approximately 30 specialized physicians who can prescribe PAH-specific therapies, such as macitentan among others.

[185] Dr. Mielniczuk's evidence was that: (i) any physician who is prescribing macitentan would be aware of the SERAPHIN data from its publication in the *New England Journal of Medicine*; and (ii) SERAPHIN was ground-breaking, as the first landmark study to show that combination therapy was effective in PAH patients. Dr. Kapasi testified that SERAPHIN was one of the first studies to include a placebo arm where patients were allowed to be on other PAH therapies. Almost two-thirds of the enrolled patients were using background therapy, and the vast majority of them were receiving a PDE5-I, often either sildenafil or tadalafil.

[186] In his report, Dr. McIvor opined that SERAPHIN established that macitentan was useful to treat PAH as a monotherapy, and that the presence of other concomitant medications used to treat PAH "did not impede its efficacy". However, in cross-examination, Dr. McIvor conceded that physicians understood SERAPHIN to establish that macitentan is safe and effective for the treatment of PAH, whether on its own or in combination with PDE5-Is:

> Q. […] My question was about what physicians understood from the Seraphin results, and I agree that they -- the one thing they would take was that macitentan itself was safe and effective for the treatment of PAH, but I'm suggesting that a second thing physicians took from Seraphin was that macitentan in combination with a PDE5 inhibitor was safe and effective; is that fair?
>
> A. If you had read and understood the trial you can't un-know what the trial tells you.
>
> Q. So is that a yes?
>
> A. That's correct, yes.
>
> Q. Okay. So it wasn't just that the safety and efficacy of macitentan wasn't impeded by the PDE5 inhibitors, it was safe and effective whether on its own or in combination, right?
>
> A. That's correct.

[187] I find that PAH specialists recognize SERAPHIN as a landmark trial that established macitentan is safe and effective alone or in combination with a PDE5-I.

[188] Based on a side-by-side comparison of the OPSUMIT and APO-MACITENTAN PMs, the APO-MACITENTAN PM does not include certain references to combination therapy that are found in the OPSUMIT PM. The "Indications and Clinical Use" section [redacted] The "Scientific Information" section [redacted]

[189] Dr. McIvor opined that a physician would understand that it is the "Indications and Clinical Use" section of the PM that sets out the details of the product in question and how it is to be used. This section of the APO-MACITENTAN PM reads:

[190] Dr. McIvor opined that the skilled person would understand this statement to be advising that APO-MACITENTAN should be taken on its own rather than in combination with other therapeutics, and in this regard, the indication for APO-MACITENTAN differs from OPSUMIT. According to Dr. McIvor, a physician would take particular note of this limitation since physicians otherwise recognize that OPSUMIT and other ERAs can be used as monotherapies and in combination with other treatments, such as PDE5-Is. A physician reviewing the APO-MACITENTAN PM would note that this representation appears to be carried through in its discussion of SERAPHIN. Dr. McIvor opined that a side-by-side comparison of the SERAPHIN results in the APO-MACITENTAN and OPSUMIT PMs shows that the APO-MACITENTAN PM only highlights the SERAPHIN results that speak to macitentan's use as monotherapy.

[191] However, the evidence does not establish that physicians would perform a side-by-side comparison between the OPSUMIT PM and the APO-MACITENTAN PM before deciding to prescribe APO-MACITENTAN. Dr. McIvor admitted that a physician would not compare brand and generic monographs, and a side-by-side comparison is an artificial exercise.

[192] Moreover, the APO-MACITENTAN PM is to be considered as a whole. In this regard, I accept the opinion of Dr. Mielniczuk that a significant portion of the information in the APO-MACITENTAN PM is the clinical trial data from SERAPHIN, which is the basis upon which physicians accept that macitentan is safe and effective in the treatment of PAH as monotherapy and in combination with PDE5-Is. I accept Dr. Mielniczuk's evidence that, while the "Indications and Clinical Use" section of the APO-MACITENTAN PM states [redacted], when read in the context of the entire PM, this statement does not suggest to physicians that they should depart from the well-established and evidence-based practice of prescribing macitentan to WHO functional class II and III PAH patients.

[193] As noted above, a majority of patients enrolled in SERAPHIN were receiving a PDE5-I. The APO-MACITENTAN PM relies on SERAPHIN data from all patients who were enrolled in the trial, including patients who were receiving combination therapy. The APO-MACITENTAN PM makes reference to the data throughout the PM and relies on them to establish the safety and efficacy of APO-MACITENTAN. The data are used to support warnings and precautions, safety data and adverse reactions, and drug interaction information for sildenafil, a PDE5-I. For example:

a) Under "Clinical Trial Adverse Drug Reactions", the APO-MACITENTAN PM includes [redacted]

b) The section on "Drug Interactions" includes [redacted] Apotex submits that an inducement to infringe generally cannot be inferred from a mere reference to the claimed use,

for example, in the course of explaining contraindications or drug interactions.. However, I find this statement to be more than a mere reference. It is one reference among others that refer to SERAPHIN data derived from all patients, including those who were on combination therapy.

c) Under the "Clinical Trials" section on pages 16-21, following the comparative bioavailability studies, the APO-MACITENTAN PM describes SERAPHIN, and includes a statement that [redacted]. The section proceeds to describe [redacted]. It also includes [redacted]

[194] Apotex argues there are no directions on how to administer APO-MACITENTAN in combination with a PDE5-I in the PM; however, such directions are also not present in the OPSUMIT PM. There was no evidence that a PAH specialist would require more than what is contained in the PM in order to prescribe macitentan in combination with a PDE5-I.

[195] Turning next to the prescribing practices of PAH specialists, Drs. Mielniczuk and Kapasi opined that physicians will review the information in the APO-MACITENTAN PM and rely on that information before prescribing APO-MACITENTAN. Dr. Mielniczuk opined that there has been little experience with generic versions of PAH drugs, and physicians will want to be satisfied that a generic medicine will provide the same safety and efficacy profile as the brand name drug. PAH is a complex and progressive disease, drug concentrations must be kept in a specific range in the body, and side effects are not inconsequential, leaving "little wiggle room" to ensure that the prescribed drug has the desired therapeutic effect. At trial, Dr. Mielniczuk testified about PAH specialists' prescribing practices:

> Now, the other point has to do with the concept of generic therapies in patients with pulmonary arterial hypertension, and there are many clinician experts, myself included, who approach generic of (sic) drugs with some trepidation. The reason for that is patients with pulmonary arterial hypertension, as I have already described, are extremely fragile patients, and even with best treatment options, unfortunately for many of our patients the disease progresses.
>
> When we are offering therapeutic decisions and therapeutic options for our patients, we want to be very confident that what we're prescribing is going to have the intended action that we anticipate from our knowledge of the drug.
>
> And so given the narrow treatment window that we have where generic drugs may have an over or an underestimate of that clinical response, that does create some ambivalence or concern on the part of the treating physicians. Particularly, as it's known, the availability of one generic medicine can be different from another generic, can be different from brand name. So anything that creates flux in the treatment pathway or the treatment effect does create some degree of uncertainty or unease for many clinicians.

[196] In Dr. McIvor's view, Drs. Kapasi and Mielniczuk ignored or understated clear differences between the OPSUMIT PM and the APO-MACITENTAN PM. In his opinion, if APO-MACITENTAN is prescribed by physicians for use with a PDE5-I in a manner akin to OPSUMIT, this would amount to an "off-label" use that does not reflect the use for APO-MACITENTAN intended by Apotex. Also, Dr. McIvor opined that physicians would not be influenced by the PM. He opined that respirologists treating PAH tend to base their prescribing decisions on their careful evaluation of the individual needs of a patient, their understanding about the drug as taught in the academic literature, information gleaned at medical conferences, and their own clinical practice rather than on the indications set out for a drug in a PM or other representations made by pharmaceutical company representatives. In these cases, physicians will either recognize that this use is "off-label" the APO-MACITENTAN PM or, indeed, may be unaware of what the APO-MACITENTAN PM even sets out. In either case, the decision will be

taken by the physician without the influence of Apotex. More simply stated, a physician will tend to do what is best for his or her patients even if it contradicts the intentions or hopes of a pharmaceutical company.

[197] I prefer the evidence of Drs. Mielniczuk and Kapasi. They are specialized physicians who treat PAH patients on a regular basis, they are highly active in this field, and they are better able to offer an opinion on PAH prescribing practices. I also find Dr. McIvor's opinion on prescribing practices to be somewhat inconsistent. On the one hand, he states that PAH physicians would take particular note of the representation that [redacted] and recognize that this representation is carried through the PM (for the reasons above, I disagree); on the other hand, he states that PAH physicians would not be influenced by the PM, he does not read PMs, and they are not a source of information for him.

[198] I find that PAH prescribing physicians will review the information in the APO-MACITENTAN PM, and rely on that information before prescribing APO-MACITENTAN.

[199] The plaintiffs have established that prescribing physicians would be influenced by the APO-MACITENTAN PM to the point that, without the influence, direct infringement would not take place. The APO-MACITENTAN PM will induce prescribing physicians to infringe claims 1-5 and 21-31 of the 770 Patent.

(c) *Corlac Test: Prong 3*

[200] The third prong of the *Corlac* test is that the influence must be knowingly exercised by the inducer. This is the knowledge that influence is being exercised, rather than knowledge that the resulting activity will infringe: *Hospira FCA* at para 45.

[201] The plaintiffs submit that knowledge can be inferred from the inducer having made and distributed the source of the influence. Apotex is in control of its APO-MACITENTAN product and the contents of the PM, which will be made available to physicians. The plaintiffs submit the evidence establishes that some physicians will be influenced to infringe: *Apotex Paliperidone* at paras 158-159. Apotex is or ought to be aware that it will exert influence over others on how its product will be used.

[202] Apotex submits the plaintiffs have failed to adduce any evidence to satisfy the knowledge requirement of the inducement test. According to Apotex, the only evidence germane to this issue is Ms. Picard's evidence, and she opined that pharmaceutical companies and health regulators would recognize that the APO-MACITENTAN PM does not authorize the marketing of APO-MACITENTAN as a combination therapy. The PM is "scrubbed clean" of any mention of combination use of macitentan with PDE5-I.

[203] I find the plaintiffs have established the third prong of the *Corlac* test. Apotex knows or ought to know that the content of the APO-MACITENTAN PM will influence physicians to complete the acts of infringement. For the reasons explained above, Apotex has not "scrubbed" its PM clean. I have not drawn an adverse inference from the fact that an Apotex witness did not

testify; however, this means there is no evidence before the Court about Apotex's efforts to remove information from the PM, and any communications with Health Canada in this regard. Ms. Picard testified that she did not speak to anyone at Apotex and she did not receive information about marketing plans for APO-MACITENTAN or how Apotex expects it to be used.

VIII. **Conclusion**

[204] The plaintiffs have not established that Apotex will infringe claims 10-20 of the 770 Patent, directly or indirectly.

[205] The plaintiffs have not established that Apotex will infringe claims 1-5 of the 770 Patent directly.

[206] The plaintiffs have established that Apotex will infringe claims 1-5 and 21-31 of the 770 Patent indirectly, by inducing physicians to infringe those claims. Apotex will influence these acts of infringement through the APO-MACITENTAN PM, with knowledge of the influence.

[207] The parties did not make cost submissions at trial. The parties advised the Court that they reached an agreement regarding a lump sum cost award and would provide a draft order. Within 7 days, the parties shall provide the draft order, together with a joint proposal and timetable for resolving any outstanding cost issues.

IX. **Postscript**

[208] Confidential Judgment and Reasons were issued to the parties on May 20, 2022, together with a Direction requesting the parties' positions on proposed redactions of any information that is confidential, and subject to the Confidentiality Order issued in this proceeding.

[209] Apotex submitted proposed redactions. The plaintiffs took the position that the Reasons should be released without redactions, as they do not contain any information which, if disclosed, would result in risk of harm that would outweigh the public interest in having the full Reasons publicly available.

[210] I disagree with the plaintiffs' position that the Reasons should be issued without redactions. However, Apotex's proposed redactions would remove more than what is defined as Confidential Information under the Confidentiality Order, and more than what is reasonably required to protect Apotex's commercial interests.

[211] The Confidentiality Order defines Confidential Information to include non-public scientific or technical information contained in the ANDS for APO-MACITENTAN filed with Health Canada, including draft PMs. The Confidentiality Order states, for greater certainty, that this includes any information related to the intended use of APO-MACITENTAN, the results of any reported clinical studies, including bioequivalence data, and results and details about the components of Apotex's APO-MACITENTAN formulation.

[212] In my view, some of Apotex's proposed redactions would delete information that is the same as or similar to information that Apotex disclosed in the public hearing, or they would delete full sentences when parts of the sentences are not confidential. Other proposed redactions would remove generalized statements about the APO-MACITENTAN PM, including opinions of expert witnesses and legal arguments of counsel that do not disclose the specific, confidential content of the APO-MACITENTAN PM.

[213] Guided by the principles set out in *Sierra Club of Canada v Canada (Minister of Finance)*, 2002 SCC 41, I find that, for certain of Apotex's proposed redactions, any potential harm to Apotex does not outweigh the public interest in open court proceedings. Furthermore, the extent of Apotex's proposed redactions would have made it difficult to understand these Reasons. When redacting reasons for a decision, the Court should consider whether redacting important parts of its reasons would render them difficult for the public to follow: *AstraZeneca Canada Inc v Apotex Inc*, 2011 FC 505 at para 177. Even where the Court agrees that information ought to be maintained in confidence, the Court should restrict the scope of redactions as much as is reasonably possible: *ibid* at para 175; see also *Mahjoub v Canada (Minister of Citizenship and Immigration)*, 2017 FCA 157 at para 29.

[214] The Court proposed more limited redactions than those proposed by Apotex, and gave the parties an opportunity to make further submissions. Apotex did not raise an issue with the more limited redactions. The plaintiffs maintained their position that there should be no redactions, and in the alternative, argued that the redactions should be even more limited than proposed. I do not accept the plaintiffs' arguments in this regard. The plaintiffs agreed to the definition of

Confidential Information under the Confidentiality Order and they do not argue that information falling within that definition should no longer be treated as confidential. The plaintiffs argue that any harm that would result from the disclosure of information in the APO-MACITENTAN PM is undermined because the PM will "inevitably" become publicly available after the 770 Patent expires—when Apotex will be free to market its APO-MACITENTAN tablets in Canada. However, the plaintiffs speculate that the APO-MACITENTAN PM at issue in this proceeding will become publicly available in the future, and in any event, if the same APO-MACITENTAN PM does become publicly available, then the appropriate recourse would be to seek an order that it should no longer be treated as Confidential Information under the Confidentiality Order.

"Christine M. Pallotta"

Judge

SCHEDULE A

Court File No: T-555-20

FEDERAL COURT

BETWEEEN:

JANSSEN INC. and ACTELION PHARMACEUTICALS LTD

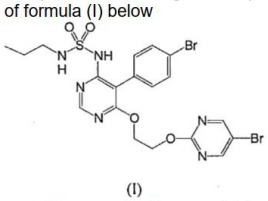
Plaintiffs

- and -

APOTEX INC.

Defendant

Parties' Joint Construction Chart for Claims 1-5 and 10-31 of Canadian Patent No. 2,659,770

Claim	Plaintiffs' Construction	Defendant's Construction
1. A product containing the compound of formula (I) below  (I) or a pharmaceutically acceptable salt of this compound, in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable salt thereof, for therapeutic use, simultaneously, separately or over a period of time, in the treatment of a disease wherein vasoconstriction is involved.	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and d) administration of (a) the product containing macitentan and (b) the PDE-5 inhibitor simultaneously, separately or over a period of time.	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and d) administration of (a) the product containing macitentan and (b) the PDE-5 inhibitor simultaneously, separately or over a period of time. The reference to combination contemplates the use of macitentan and PDE-5 inhibitor where this is something that a doctor intended at the outset of treatment and where it would be understood that the two drugs are working in concert to treat the disease in question. The terms simultaneously, separately or over a period of time receive the interpretation supplied by the disclosure.

Claim	Plaintiffs' Construction	Defendant's Construction
2. A product according to claim 1, wherein the compound having PDE5-inhibitory properties is sildenafil, vardenafil, tadalafil or udenafil.	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with sildenafil, vardenafil, tadalafil or udenafil (or their pharmaceutically acceptable salt); c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and d) administration of (a) the product containing macitentan and (b) the sildenafil, vardenafil, tadalafil or udenafil simultaneously, separately or over a period of time.	Same essential elements (a)-(d) as in claim 1, save for that the PDE-5 inhibitor of element (b) is one of sildenafil, vardenafil, tadalafil or udenafil or their pharmaceutically acceptable salts.
3. A product according to claim 2, wherein the compound having PDE5-inhibitory properties is tadalafil.	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with tadalafil (or its pharmaceutically acceptable salt); c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; and d) administration of (a) the product containing macitentan and (b) the	Same essential elements (a)-(d) as in claim 2, save for that the PDE-5 inhibitor of element (b) is tadalafil or its pharmaceutically acceptable salts.

Claim	Plaintiffs' Construction	Defendant's Construction
	tadalafil simultaneously, separately or over a period of time.	
4. A product according to claim 2, wherein the compound having PDE5-inhibitory properties is sildenafil.	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with sildenafil (or its pharmaceutically acceptable salt); c) for therapeutic use in the treatment of a disease where vasoconstriction is involved; d) administration of (a) the product containing macitentan and (b) the sildenafil simultaneously, separately or over a period of time.	Same essential elements (a)-(d) as in claim 2, save for that the PDE-5 inhibitor of element (b) is sildenafil or its pharmaceutically acceptable salts.
5. A product according to claim I, wherein the disease wherein vasoconstriction is involved is hypertension, pulmonary hypertension, diabetic arteriopathy, heart failure, erectile dysfunction or angina pectoris.	a) a product containing macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) for therapeutic use in the treatment of hypertension, pulmonary hypertension (including pulmonary arterial hypertension), diabetic arteriopathy,	Same essential elements (a)-(d) as in claim 1, save for that the diseases in which vasoconstriction is involved are limited to hypertension, pulmonary hypertension, diabetic arteriopathy, heart failure, erectile dysfunction or angina pectoris.

Claim	Plaintiffs' Construction	Defendant's Construction
	heart failure, erectile dysfunction or angina pectoris; d) administration of (a) the product containing macitentan and (b) the PDE-5 inhibitor simultaneously, separately or over a period of time.	
10. A use of the compound of formula (1) as defined in claim 1, or a pharmaceutically acceptable salt of said compound of formula (1), in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament intended to treat a disease wherein vasoconstriction is involved.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat a disease where vasoconstriction is involved.	a) use of macitentan or its pharmaceutically acceptable salt for the manufacture of a medicament; b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat a disease where vasoconstriction is involved. The claim requires that macitentan be used in combination with a PDE-5 inhibitor to treat a disease where vasoconstriction is involved. The term combination would be interpreted in the same manner as in claim 1.

Claim	Plaintiffs' Construction	Defendant's Construction
11. The use according to claim 10, wherein the compound having PDE5-inhibitory properties is sildenafil, vardenafil, tadalafil or udenafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with sildenafil, vardenafil, tadalafil or udenafil (or their pharmaceutically acceptable salt); c) where the medicament is intended to treat a disease where vasoconstriction is involved.	Same essential elements as claim 10, save for that the PDE-5 inhibitor to be used is one of sildenafil, vardenafil, tadalfil or udenafil or their pharmaceutically acceptable salts).
12. The use according to claim 11, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with sildenafil or tadalafil (or their pharmaceutically acceptable salt); c) where the medicament is intended to treat a disease where vasoconstriction is involved.	Same essential elements as claim 11, save for that the PDE-5 inhibitor to be used is sildenafil or tadalafil or their pharmaceutically acceptable salts.
13. The use according to claim 12, wherein the compound having PDE5-inhibitory properties is sildenafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament;	Same essential elements as claim 11, save for that the PDE-5 inhibitor to be used is sildenafil or its pharmaceutically acceptable salts.

Claim	Plaintiffs' Construction	Defendant's Construction
	b) in combination with sildenafil (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat a disease where vasoconstriction is involved.	
14. The use according to claim 12, wherein the compound having PDE5-inhibitory properties is tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with tadalafil (or pharmaceutically acceptable its salt); c) where the medicament is intended to treat a disease where vasoconstriction is involved.	Same essential elements as claim 11, save for that the PDE-5 inhibitor to be used is tadalafil or its pharmaceutically acceptable salts.
15. The use according to claim 10, wherein the disease intended to be treated is hypertension or pulmonary hypertension.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat hypertension or pulmonary hypertension (including pulmonary arterial hypertension).	Same essential elements as claim 10, save for that the diseases to be treated are hypertension or pulmonary hypertension.

Claim	Plaintiffs' Construction	Defendant's Construction
16. The use according to claim 15, wherein the disease intended to be treated is pulmonary hypertension.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat pulmonary hypertension (including pulmonary arterial hypertension).	Same essential elements as claim 15, save for that the disease to be treated is pulmonary hypertension.
17. The use according to claim 16, wherein the disease intended to be treated is pulmonary arterial hypertension.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat pulmonary arterial hypertension.	Same essential elements as claim 16, save for that the disease to be treated is pulmonary arterial hypertension.
18. The use according to claim 17, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with sildenafil or tadalafil (or its pharmaceutically acceptable salt);	Same essential elements as claim 17, save for that the PDE-5 inhibitor is one of sildenafil or tadalafil.

Claim	Plaintiffs' Construction	Defendant's Construction
	c) where the medicament is intended to treat pulmonary arterial hypertension.	
19. The use according to claim 17, wherein the compound having PDE5-inhibitory properties is sildenafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with sildenafil (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat pulmonary arterial hypertension.	Same essential elements as claim 17, save for that the PDE-5 inhibitor is sildenafil.
20. The use according to claim 17, wherein the compound having PDE5-inhibitory properties is tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt) for the manufacture of a medicament; b) in combination with tadalafil (or its pharmaceutically acceptable salt); c) where the medicament is intended to treat pulmonary arterial hypertension.	Same essential elements as claim 17, save for that the PDE-5 inhibitor is tadalafil.
21. A use of the compound of formula (1) as defined in claim 1, or a pharmaceutically acceptable salt of said compound of formula (1), in combination with at least one compound having PDE5-inhibitory properties, or a pharmaceutically	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt);	a) use of macitentan or its pharmaceutically acceptable salt; b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt);

Claim	Plaintiffs' Construction	Defendant's Construction
acceptable salt thereof, for treating a disease wherein vasoconstriction is involved.	c) for treating a disease where vasoconstriction is involved.	c) for treating a disease where vasoconstriction is involved. The term combination would be interpreted as in the case for claim 1.
22. The use according to claim 21, wherein the compound having PDE5-inhibitory properties is sildenafil, vardenafil, tadalafil or udenafil.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with sildenafil, vardenafil, tadalafil or udenafil (or their pharmaceutically acceptable salt); c) for treating a disease where vasoconstriction is involved.	Same as claim 21, save for that the PDE-5 inhibitors are sildenafil, vardenafil, tadalfil or udenafil.
23. The use according to claim 22, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with sildenafil or tadalafil (or their pharmaceutically acceptable salt); c) for treating a disease where vasoconstriction is involved.	Same as claim 21, save for that the PDE-5 inhibitors are sildenafil or tadalafil.
24. The use according to claim 23, wherein the compound having PDE5-inhibitory properties is sildenafil.	a) use of macitentan (or its pharmaceutically acceptable salt);	Same as claim 21, save for that the PDE-5 inhibitor is sildenafil.

Claim	Plaintiffs' Construction	Defendant's Construction
	b) in combination with sildenafil (or its pharmaceutically acceptable salt); c) for treating a disease where vasoconstriction is involved.	
25. The use according to claim 23, wherein the compound having PDE5-inhibitory properties is tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with tadalafil (or its pharmaceutically acceptable salt); and c) for treating a disease where vasoconstriction is involved.	Same as claim 21, save for that the PDE-5 inhibitor is tadalafil.
26. The use according to claim 21, wherein the disease is selected from hypertension and pulmonary hypertension.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) for treating hypertension or pulmonary hypertension (including pulmonary arterial hypertension).	Same as claim 21, save for that the disease state is hypertension or pulmonary hypertension.
27. The use according to claim 26, wherein the disease is pulmonary hypertension.	a) use of macitentan (or its pharmaceutically acceptable salt);	Same as claim 26, save for that the disease state is pulmonary hypertension.

Claim	Plaintiffs' Construction	Defendant's Construction
	b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) for treating pulmonary hypertension (including pulmonary arterial hypertension).	
28. The use according to claim 27, wherein the disease is pulmonary arterial hypertension.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with at least one PDE-5 inhibitor (or its pharmaceutically acceptable salt); c) for treating pulmonary arterial hypertension.	Same as claim 27, save for that the disease state is pulmonary arterial hypertension.
29. The use according to claim 28, wherein the compound having PDE5-inhibitory properties is sildenafil or tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with sildenafil or tadalafil (or their pharmaceutically acceptable salt); c) for treating pulmonary arterial hypertension.	Same as claim 28, save for that the PDE-5 inhibitor is sildenafil or tadalfil.
30. The use according to claim 28, wherein the compound having PDE5-inhibitory properties is sildenafil.	a) use of macitentan (or its pharmaceutically acceptable salt);	Same as claim 28, save for that the PDE-5 inhibitor is sildenafil.

Claim	Plaintiffs' Construction	Defendant's Construction
	b) in combination with sildenafil (or its pharmaceutically acceptable salt); c) for treating pulmonary arterial hypertension.	
31. The use according to claim 28, wherein the compound having PDE5-inhibitory properties is tadalafil.	a) use of macitentan (or its pharmaceutically acceptable salt); b) in combination with tadalafil (or its pharmaceutically acceptable salt); c) for treating pulmonary arterial hypertension.	Same as claim 28, save for that the PDE-5 inhibitor is sildenafil.

FEDERAL COURT

SOLICITORS OF RECORD

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