Federal Court Cour fédérale

Date: 20180730

Docket: T-1921-17

Citation: 2018 FC 694

Ottawa, Ontario, July 30, 2018

PRESENT: Case Management Judge Mandy Aylen

BETWEEN:

GENENTECH, INC. AND HOFFMANN-LA ROCHE LIMITED

Plaintiffs

and

AMGEN CANADA INC.

Defendant

PUBLIC ORDER
(Confidential Order issued July 6, 2018)

[1] On this motion, the Defendant, Amgen Canada Inc. [Amgen], seeks an order pursuant to section 6.08 of the *Patented Medicines (Notice of Compliance) Regulations* [*Regulations*] dismissing this action in respect of Canadian Patent Nos. 2,376,596 [596 Patent] and 2,407,556 [556 Patent] on the ground that the action is redundant, scandalous, frivolous or vexatious or is otherwise an abuse of process. Specifically, Amgen asserts that there is insufficient evidence to support the claims in relation to the 596 and 556 Patents and as such, the claims are so clearly

futile that they have not the slightest chance of success. For the reasons that follow, the motion is dismissed with costs to the Plaintiffs in any event of the cause.

Background

[2] This action pertains to HERCEPTIN (trastuzumab) which is marketed in Canada by the Plaintiff, Hoffmann-La Roche Limited [Roche] for the treatment of early breast cancer [EBC], metastatic breast cancer [MBC] and gastric cancer.

(a) The Patents at Issue

[3] Since HERCEPTIN was first approved in approximately 1999, Roche has listed six patens on the Patent Register, which patents are owned by the Plaintiff, Genentech, Inc.. One of those patents, Canadian Patent No. 2,311,409, claims the use of trastuzumab to treat HER2+ breast cancer, including MBC and including in combination with docetaxel, and is set to expire by the end of this year. Another patent, Canadian Patent No. 1,341,082, which claims the trastuzumab antibody itself, has already expired.

[4] Four other patents are at issue in this action and two are at issue on this motion – namely, the 596 Patent and the 556 Patent.

[5] The 596 Patent is entitled “Humanized anti-ErbB2 antibodies and treatment with anti-ErbB2 antibodies”. The 596 Patent contains 49 claims, of which claim 1 is the only independent claim. The asserted claims of the 596 Patent (claims 23-27) depend, directly or indirectly, from claim 1. Claim 1 claims an antibody which comprises the variable heavy (V_H) domain amino acid sequence set forth in SEQ ID NO:4 and the variable light (V_L) domain amino acid sequence set forth in SEQ ID NO:3. Claim 2 claims the antibody of claim 1 which is an intact I_gG1 antibody,

which the Plaintiffs assert includes the monoclonal antibody known as rhuMAb2C4, also known as pertuzumab, which is sold by Roche as PERJETA. Claim 3 claims the antibody of claim 1, which is an antibody fragment. Claim 4 claims the antibody of claim 3, which is a Fab fragment.

[6] Claim 19 claims the use of the antibody of any one of claims 1 to 4 in the manufacture of a medicament for treating breast cancer. Claim 20 claims the use of the antibody of any one of claims 1 to 4 for treating breast cancer. Claim 21 claims the use according to claim 19 or 20, wherein the breast cancer is metastatic breast cancer. Claim 22 claims the use according to claim 19, 20 or 21, wherein the breast cancer overexpresses HER2.

[7] Claims 23 and 24 claim the use according to any one of claims 19 to 22, wherein the medicament is for use in combination with a second antibody which binds ErbB2 and inhibits growth of cancer cells which overexpress ErbB2. According to the Plaintiffs, ErbB2 is also known as HER2. Claim 24 specifies that the second antibody is huMAb4D5-8, which the Plaintiffs assert is also known as trastuzumab, which is sold by Roche as HERCEPTIN.

[8] Claims 25 to 27 claim the use according to claim 24, wherein rhuMAb4D5-8 is for use before, following or simultaneously with rhuMAb2C4, respectively.

[9] The parties all agree that the standard of care for first-line HER2+ MBC treatment is based on the CLEOPATRA clinical trial. In that trial, the triple combination of trastuzumab, pertuzumab (PERJETA) and docetaxel was compared to the double combination of trastuzumab and docetaxel. At the time of the study, the double combination was the standard of care. The CLEOPATRA study revealed that a typical HER2+ MBC patient will live approximately 15.7 months longer if given the triple combination of trastuzumab, pertuzumab and docetaxel as first-

line therapy. As such, oncologists in Canada prescribe a triple combination of trastuzumab, pertuzumab and a taxane (either paclitaxel or docetaxel) in first-line treatment of HER2+ MBC patients.

[10] The HERCEPTIN product monograph includes a reference to the current standard of care, where it provides:

> **Metastatic Breast Cancer (MBC)**
>
> HERCEPTIN is indicated for the treatment of patients with MBC whose tumours overexpress HER2.
>
> […]
>
> HERCEPTIN can be used in combination with PERJETA® (pertuzumab) and docetaxel for the treatment of patients with HER2-positive metastatic breast cancer who have not received prior anti-HER2 therapy or chemotherapy for metastatic disease…

[11] The 556 Patent is entitled "Gene detection assay for improving the likelihood of an effective response to an ErbB antagonist cancer therapy". The 556 Patent contains 13 claims, of which claims 1, 2, 7, 8 and 9 are independent claims. The Plaintiffs assert that each and every claim of the 556 Patent will be infringed by Amgen.

[12] Claim 1 claims the use of an ErbB antagonist which is an anti-HER2 protein antibody in the manufacture of a medicament for treating a breast cancer in a subject, wherein the subject is one for whom a *her2* gene in tumor cells in a tissue sample from the subject has been found to be amplified and the subject's tumor cells have HER2 expression level of 0 or 1+ by immunohistochemistry on a formaldehyde-fixed tissue sample.

[13] Claim 2 claims the use of an effective amount of an ErbB antagonist which is an anti-HER2 protein antibody for treating a breast cancer in a subject, wherein the subject is one for whom a *her2* gene in tumor cells in a tissue sample from the subject has been found to be amplified and the subject's tumor cells have HER2 expression level of 0 or 1+ by immunohistochemistry on a formaldehyde-fixed tissue sample.

[14] Claim 3 claims a use according to claim 1 or 2, wherein the antibody is recombinant humanized monoclonal antibody rhuMAb 4D5-8, which the Plaintiffs assert is also known as trastuzumab.

[15] Claim 4 claims the use according to any one of claims 1 to 3, wherein the *her2* gene amplification is detected by detecting fluorescence of a fluorescence-labeled nucleic acid probe hybridized to the gene.

[16] Claim 5 claims the use according to any of claims 1 to 4, wherein the ErbB antagonist is for use with a chemotherapeutic drug. Claim 6 depends from claims 1 to 5 and specifies that the chemotherapeutic drug is a taxoid.

[17] Claim 7 claims a method for identifying a patient disposed to respond favorably to an ErbB antagonist for treating a breast cancer, wherein the ErbB antagonist is an anti-HER2 protein antibody, which method comprises detecting *her2* gene amplification in tumor cells in a tissue sample from the patient, wherein the patient's tumor cells have HER2 expression level of 0 or 1+ by immunohistochemistry on a formaldehyde-fixed tissue sample.

[18] Claim 8 claims an ErbB antagonist for use in treating a breast cancer in a subject, wherein the ErbB antagonist is an anti-HER2 protein antibody, wherein the subject is one for

whom a *her2* gene in tumor cells in a tissue sample from the subject has been found to be amplified and the subject's tumor cells have HER2 expression level of 0 or 1+ by immunohistochemistry on a formaldehyde-fixed tissue sample.

[19] Claim 9 claims an ErbB antagonist for use in formulating a medicament for treating a breast cancer in a subject, wherein the ErbB antagonist is an anti-HER2 protein antibody, wherein the subject is one for whom a *her2* gene in tumor cells in a tissue sample from the subject has been found to be amplified and the subject's tumor cells have HER2 expression level of 0 or 1+ by immunohistochemistry on a formaldehyde-fixed tissue sample.

[20] Claim 10 depends from either claim 8 or claim 9 and specifies that the antibody is recombinant humanized monoclonal antibody rhuMab 4D5-8 (trastuzumab).

[21] Claim 11 depends from any one of claims 8 to 10 and specifies that the *her2* gene amplification is detected by detecting fluorescence of a fluorescent-labeled nucleic acid probe hybridized to the gene.

[22] Claim 12 depends from any one of claims 8 to 11 and specifies that the ErbB antagonist is for use with a chemotherapeutic drug.

[23] Claim 13 depends from claim 12 and specifies that the chemotherapeutic drug is a taxoid.

[24] With respect to the testing and selection of patients eligible for trastuzumab treatment, the parties generally agree that:

A. HER2 overexpression is determined by subjecting a formaldehyde-fixed tumour sample to immunohistochemistry [IHC]. HER2 expression by IHC is measured on a scale of 0 to 3+.

B. Amplification of the *her2* gene is determined by subjecting a formaldehyde-fixed tumour sample to in situ hybridization [ISH]. A common type of ISH assay is fluorescent ISH [FISH]. Amplification of the *her2* gene can be denoted as ISH+.

C. A tumour that is IHC 3+ is considered HER2+. A tumour that is IHC 2+ is considered equivocal and will normally be sent for further testing to determine if the cells have *her2* gene amplification. A tumour that is IHC 0 or 1+ is not considered to overexpress HER2 and will not typically be sent for further testing.

[25] Under the heading "Selection of Patients/Diagnostic Tests", the HERCEPTIN product monograph provides:

> HERCEPTIN should only be used in patients whose tumours overexpress HER2 as determined by immunohistochemistry. CICH or FISH testing for HER2 status also may be used, provided that the testing is done in experienced laboratories that have validated the test.

(b) Amgen's New Drug Submission for KANJINTI

[26] Amgen filed a new drug submission to obtain a notice of compliance for a product that Amgen refers to as KANJINTI or ABP 980, a biosimilar of trastuzumab.

[27] In its notice of allegation, Amgen seeks to market KANJINTI for the same indications as HERCEPTIN – namely, EBC, MBC and gastric cancer. Amgen asserts that it will not infringe the 596 and 556 Patents and that both patents are invalid. Specifically, Amgen asserts that it will

not infringe the 596 Patent because it is not seeking approval for the use of KANJINTI in combination with PERJETA (pertuzumab). In that regard, Amgen says that it has expressly carved out PERJETA combination therapy from its draft product monograph.

[28] With respect to the 596 Patent, Amgen asserts that while the draft product monograph for KANJINTI provides some options for testing for HER2 overexpression, those testing options have been available and used since HERCEPTIN's original approval and the manner in which a patient's HER2 status is determined will play no part whatsoever in Amgen's marketing plans for KANJINTI.

[29] The key portions of the draft product monograph for KANJINTI provide as follows:

> **Metastatic Breast Cancer (MBC)**
>
> [redacted]
>
> […]
>
> [redacted]
>
> […]
>
> **Selection of Patients/Diagnostic Tests**
>
> […]
>
> KANJINTI should only be used in patients whose tumours overexpress HER2 as determined by immunohistochemistry. CICH or FISH testing for HER2 status also may be used, provided that the testing is done in experienced laboratories that have validated the test.

(c) Section 6 Action

[30] On December 11, 2017 and in response to the notice of allegation, the Plaintiffs commenced this action pursuant to section 6 of the *Regulations*, seeking an order prohibiting the Minister from issuing a notice of compliance to Amgen for KANJINTI until after the expiry of the 596 and 556 Patents.

(d) Evidence on this Motion

[31] In support of this motion, Amgen filed the affidavit of John Snowden, the Director of Biosimilars at Amgen. The key portions of Mr Snowden's evidence are as follows:

A. He is responsible for all aspects of the commercialization of the biosimilar portfolio in development at Amgen and supervises the marketing for Amgen's biosimilars, including KANJINTI.

B. Amgen is seeking approval from Health Canada for two indications for KANJINTI relating to the treatment of breast cancer: (i) treatment of patients with EBC with ECOG 0-1 status, whose tumours overexpress HER2, following surgery and after chemotherapy, following adjuvant chemotherapy consisting of doxorubicin and cyclophosphamide, in combination with paclitaxel or docetaxel and in combination with adjuvant chemotherapy consisting of docetaxel and carboplatin; and (ii) treatment of patients with MBC whose tumours overexpress HER2.

C. Amgen has not sought approval for use of KANJINTI in combination with PERJETA and its product monograph makes no reference to PERJETA or pertuzumab.

D. In [redacted], Amgen decided that its new drug submission would not seek approval for KANJINTI in combination with PERJETA, [redacted] - Amgen will not market or in any way promote the use of KANJINTI for combination therapy with PERJETA.

E. KANJINTI will be indicated for patients that overexpress HER2, but Amgen will not encourage or market any particular test or method to determine which patients have tumours that overexpress HER2. Other than the above-reference in the KANJINTI draft product monograph, the method for testing for HER2 overexpression or HER2 status plays no part in Amgen's marketing plans for KANJINTI.

F. Amgen will submit all of its marketing material for KANJINTI to the Canadian Pharmaceutical Advertising Advisory Board. While no material has yet been submitted, that material will not refer to combined administration with PERJETA

or any particular test methods to determine whether a patient's tumour overexpresses HER2 (other than what is in the draft product monograph).

G. Amgen has not yet made any applications to CADTH, CADTH's pan-Canadian Oncology Drug Review, provincial cancer agencies or to any other agency or institution in relation to market access and reimbursement for KANJINTI. However, when such applications are ultimately made, they will not refer to combined administration with PERJETA or any particular test methods to determine whether a patient's tumour overexpresses HER2 (other than what is in the draft product monograph). The only efforts undertaken by Amgen related to a reimbursement strategy for KANJINTI have been limited to a biosimilar consultancy meeting held with pharmacists in November 2017.

H. Amgen does not currently have any marketing materials for KANJINTI and its current marketing plans are contained within its launch plan, which was updated in March 2018. The launch plan contains no references to any market strategy for use of KANJINTI in combination with PERJETA.

I. Amgen has global marketing documents for KANJINTI developed by Amgen's global affiliate for adaptation and use by local Amgen entities [Global Documents]. The Global Documents are in draft form and are intended to provide a template for the appearance and organizational structure of promotional and educational materials regarding KANJINTI. Some of the Global Documents may be used in Canada in some form, although Amgen has not yet evaluated which are appropriate for Canada. However, any Global Documents used in Canada will be

specifically adapted to ensure that they accord with the product monograph for KANJINTI.

J. Amgen held a consultancy meeting with Canadian physicians on October 6, 2017 to obtain feedback and gather recommendations on a variety of topics, including physician's attitudes to biosimilars in general and potential trastuzumab biosimilars, how to communicate information to Canadian oncologists and how physicians would perceive and prescribe a trastuzumab biosimilar product in the short and long term. The meeting was originally planned for the spring of 2017, at a time when Amgen had not yet decided to not seek approval for combination therapy with PERJETA. As such, a number of the documents related to the meeting address pertuzumab. However, no questions were asked by Amgen about pertuzumab at the meeting itself.

[32] Amgen also relied on the affidavit of Diane Zimmerman, a law clerk, to which was appended the patents at issue in this proceeding, copies of certain productions made by the parties and various other documents.

[33] The Plaintiffs have filed expert evidence in the form of an affidavit from Dr. Eitan Amir, a medical oncologist at Princess Margaret Cancer Centre and Mount Sinai Hospital in Toronto and an Associate Professor at the University of Toronto, Department of Medicine (Medical Oncology Division) and Institute of Health Policy, Management and Evaluation. His clinical practice is focused on breast cancer and his academic practice is focused on health services research in cancer medicine. The key portions of Dr. Amir's evidence are as follows:

A. It is his opinion that Amgen is seeking Health Canada's approval to use KANJINTI for HER2+ MBC, including for first-line treatment of HER2+ MBC and will inform medical oncologists of same. It would be inconsistent with the standard of care to not use a combination of KANJINTI and PERJETA for first-line treatment of HER2+ MBC. As a result, if KANJINTI is approved by Health Canada for the indications in the KANJINTI draft product monograph, KANJINTI will be prescribed by some medical oncologists for use in combination with PERJETA.

B. The second paragraph of the KANJINTI product monograph – that states [redacted]

C. [redacted]

D. Other documents that he reviewed support his view that Amgen is endorsing the use of KANJINTI in combination with PERJETA. AMG434 entitled "The KANJINTI [redacted]" (and which is one of the Global Documents) [redacted] sets out how Amgen representatives are to respond to questions and concerns raised by medical oncologists. On page 13, the document raises the following question – [redacted]. Under the heading "support" below the response, it states [redacted]

[redacted]

E. Various other statements in the KANJINTI [redacted]

[redacted]

F. [redacted]

[redacted] These statements are a reassurance by Amgen to medical oncologists that the use of KANJINTI in the place of HERCEPTIN for all MBC regimens is acceptable.

G. It is his opinion that KANJINTI will be prescribed in Canada for breast cancer patients for whom a *her2* gene in their tumour cells has been found to be amplified and their tumour cells have HER2 expression level of 0 or 1+ by immunohistochemistry on a formaldehyde-fixed tissue sample. These patients currently receive HERCEPTIN. Amgen is seeking to have KANJINTI approved for all HERCEPTIN indications and will not seek a carve out for IHC 0/1+ ISH+ patients in its product monograph, nor are there any express statements excluding these patients from treatment with KANJINTI. The product monograph and Amgen's documents will inform medical oncologists that KANJINTI is appropriate for all HER2+ breast cancer patients, including IHC 0/1+ ISH+ patients.

H. In Canada, the standard approach is to test a tumour with IHC first, with IHC 0/1+ being considered HER2-negative, IHC 3+ being considered HER2+ and IHC 2+ being considered equivocal. Equivocal IHC cases are then sent for reflex ISH testing. Despite this standard approach and based on his personal experience, IHC 1+ samples are occasionally send for ISH testing. There are a number of reasons why an IHC 1+ sample may be sent for ISH testing and only a small percentage

will turn out to be ISH+ (2% based on a recent study). Accordingly, there are breast cancer patients with tumours that show *her2* gene amplification by ISH despite having apparently normal HER2 expression levels by IHC (i.e. a score of 0 or 1+).

I. Of the estimated 26,300 Canadian women who were diagnosed with breast cancer in 2017, approximately 4,103 women will be HER2+ and of those HER2+ women, approximately 27 will be IHC 0/1+ ISH+.

J. The standard of care for IHC 0/1+ ISH+ patients is HERCEPTIN (if the patient otherwise qualifies).

K. The KANJINTI draft product monograph and Amgen's documentation show that Amgen does not intend to exclude IHC 0/1+ ISH+ patients from the indications it is seeking for KANJINTI. Rather, Amgen intends to promote KANJINTI to medical oncologists as a safe and effective alternative to HERCEPTIN for all indications, including this sub-set of patients.

L. The KANJINTI draft product monograph states that it "should only be used in patients whose tumours overexpress HER2 as determined by immunohistochemistry. CICH or FISH testing for HER2 status also may be used, provided that the testing is done in experienced laboratories that have validated the test". This means that a positive ISH test is sufficient to prescribe KANJINTI for HER2+ breast cancer. The reference to CISH and FISH would be interpreted by a medical oncologist as a reference to any acceptable ISH testing. A medical

oncologist would therefore understand that a patient with IHC 0/1+ ISH+ breast cancer can be prescribed KANJINTI regardless of its IHC score.

M. The KANJINTI [redacted] includes on page 4 the question – [redacted]

[redacted]

Amgen's intended answer states [redacted]

[redacted]

N. Once KANJINTI is approved, medical oncologists will prescribe it for HER2+ breast cancer patients and a small percentage of those patients will be IHC 0/1+ ISH+ patients.

[34] The Plaintiffs have also filed expert evidence in the form of an affidavit from Sherry O'Quinn, a pharmacist by training and the Managing Principal and co-founder of Mani & O'Quinn Reimbursement Strategy Experts (MORSE) Consulting Inc., a consulting firm that

provides market access and reimbursement strategies for clients in the pharmaceutical and health care industries. For approximately 13 years, Ms. O'Quinn worked at the Ontario Public Drugs Program, Ministry of Health and Long-Term Care, supporting decision making for the public funding of drugs, including oncology drugs and biosimilars. The key portions of Ms. O'Quinn's evidence are as follows:

A. It is her opinion that a public payer will list KANJINTI with identical reimbursement criteria to those of HERCEPTIN. This will include the use of KANJINTI in combination with pertuzumab for the treatment of MBC.

B. In Canada, the majority of intravenous cancer drugs, such as trastuzumab, are funded by public payers such as provincial drug plans and cancer agencies. The same will be true for oncology biosimilars. As such, Amgen needs a robust market access strategy in order to achieve meaningful sales and commercial success. A key element of that strategy will be to secure, at minimum, broad funding criteria across all indications, the same as those for the innovator biologic. It will also be important for Amgen to begin discussions with public payers early, even before the official reimbursement process has begun.

C. As Amgen is seeking approval of Kajinti for all available indications of HERCEPTIN, it is her expectation that Amgen will seek reimbursement criteria identical to that of HERCEPTIN for those indications. HERCEPTIN is currently funded for all of its indications, including various treatment regimens for MBC that include trastuzumab with pertuzumab.

D. The key issue for a public payer is whether it can fund the biosimilar for the same indications as the reference biologic. KANJINTI is indicated for the same indications as HERCEPTIN – EBC, MBC and metastatic gastric cancer. The treatment regimen for the two drugs is almost identical, with the exception of the reference to PERJETA. A public payer would ask why the reference to PERJETA was removed, particularly in light of the fact that the current standard of care for first-line MBC is trastuzumab in combination with pertuzumab and a taxane. In answer to this question, she considered the KANJINTI [redacted] (and in particular, the question on page 13 as detailed above) and the [redacted] (and in particular, the question on page 10 as detailed above). In relation to the [redacted], the document also asks at page 10 [redacted] and the response provided is [redacted]. These answers would inform and satisfy a public payer that KANJINTI, like HERCEPTIN, can be funded in combination with PERJETA.

E. If KANJINTI could not be used in combination with PERJETA, she would expect that Amgen would explicitly advise the payer of this information. There is no such disclaimed and to the contrary, Amgen has stated that KANJINTI can be used in the same manner as HERCEPTIN.

F. Having reviewed the affidavit of John Snowden filed by Amgen in support of this motion, his evidence does not affect her opinion.

[35] The Plaintiffs also rely on the affidavit of Christian Landeta, a law clerk, appended to which are a number of Amgen's productions and other documents.

[36] Mr. Snowden, Dr. Amir and Ms. O'Quinn were each cross-examined on their affidavits and the transcripts of their respective cross-examinations were provided to the Court.

Analysis

[37] This is the first motion that has been brought before this Court pursuant to section 6.08 of the new *Regulations*. Section 6.08 provides:

An action brought under subsection 6(1) may, on the motion of a second person, be dismissed, in whole or in part, on the ground that it is redundant, scandalous, frivolous or vexatious or is otherwise an abuse of process in respect of one or more patents or certificates of supplementary protection.	Toute action intentée en vertu du paragraphe 6(1) peut, sur requête de la seconde personne, être rejetée en tout ou en partie au motif qu'elle est inutile, scandaleuse, frivole ou vexatoire ou qu'elle constitue par ailleurs un abus de procédure à l'égard d'un ou de plusieurs brevets ou certificats de protection supplémentaire.

[38] The language in section 6.08 is essentially the same as the language in section 6(5)(b) of the earlier version of the *Regulations,* which provided:

Subject to subsection (5.1), in a proceeding in respect of an application under subsection (1), the court may, on the motion of a second person, dismiss the application in whole or in part	Sous réserve du paragraphe (5.1), lors de l'instance relative à la demande visée au paragraphe (1), le tribunal peut, sur requête de la seconde personne, rejeter tout ou partie de la demande si, selon le cas:

(b) on the ground that it is redundant, scandalous, frivolous or vexatious or is otherwise an abuse of process in respect of one or more patents	b) il conclut qu'elle est inutile, scandaleuse, frivole ou vexatoire ou constitue autrement, à l'égard d'un ou plusieurs brevets, un abus de procédure.

[39] As the drafters of the *Regulations* retained the Court's discretion to strike proceedings at a preliminary stage on the ground that a claim asserted in relation to a particular patent is redundant, scandalous, frivolous, vexatious or otherwise an abuse of process, I see no reason why the jurisprudence under section 6(5)(b) of the prior version of the *Regulations* would not apply on a section 6.08 motion.

[40] However, in reaching this conclusion, I am mindful that certain commentary and findings made in the section 6(5)(b) case law were influenced, at least in part, by the fact that those proceedings were applications and the first person did not have the benefit of documentary or oral discovery. Under the current *Regulations*, it should, in theory, be easier for a plaintiff to resist a section 6.08 motion and for a defendant to prosecute a section 6.08 motion as all parties will have had the benefit of documentary productions and possibly examinations for discovery (depending on the timing of the motion) to bolster the strength of their respective positions. In that regard, while the product monograph for the proposed product was the key document in prior section 6 applications, the product monograph is now one of many potentially key documents in a section 6 action.

[41] In approaching section 6.08 motions, the Court must also be mindful that the consequences of granting a section 6.08 motion are more significant than motions previously granted under section 6(5)(b). Where a motion was granted under section 6(5)(b), an applicant still had the ability to commence an action against a respondent for infringement of the

applicant's patent once the respondent's proposed product that was the subject of the notice of allegation came to market.

[42] However, in the case of a section 6.08 motion, if a plaintiff's claim is struck, the plaintiff is precluded, by virtue of section 6.01 of the *Regulations*, from commencing an action against the defendant for infringement of a patent that is the subject of the notice of allegation in relation to the making, constructing, using or selling of a drug in accordance with the submission. As such, the Court should now exercise a heightened level of caution in striking claims pursuant to section 6.08 of the *Regulations* and such motions should be granted only in the clearest of cases.

[43] As set out in the section 6(5)(b) case law, striking an action pursuant to section 6.08 of the *Regulations* remains an extraordinary remedy and the threshold on such a motion is high. The moving party bears the onus of demonstrating that the claim is "so clearly futile that it has not the slightest chance of success" or, put differently, that it is "plain and obvious" that the claim has no chance of success [*Bayer Inc v Pharmaceutical Partners of Canada Inc*, 2015 FC 388, aff'd 2015 FC 797; *Bristol-Myers Squibb Canada v Apotex Inc*, 2017 FC 1061].

[44] Substantive arguments regarding non-infringement should, as a general rule, be addressed at the trial. This Court has repeatedly discouraged this type of motion where the motion relies on lengthy submissions, contradictory jurisprudence and contentious points of fact and law [*Nycomed Canada Inc v Novopharm Limited*, 2008 FC 454 at para 31 and 32; *Valeant Canada LP v Canada (Health)*, 2013 FC 1254 at para 38; *Nycomed GMBH v Canada (Health)*, 2008 FC 330 at paras 4 and 78].

[45] A defendant may move to dismiss the action on the basis that a plaintiff's evidence is insufficient to prove a defendant's allegations of infringement are not justified. In order to make such a determination, the Court must be able to make the necessary findings of fact, viewed in the light most favourable to the plaintiff and apply the law to the facts [*Bayer Inc v Pharmaceutical Partners of Canada Inc, supra* at para 17, aff'd 2015 FC 797].

[46] However, it is critical to keep in mind that a section 6.08 motion, like a motion under Rule 221 of the *Federal Courts Rules*, is not a hearing on the merits. The Court's role is not to determine whether there has been infringement or inducement and the Court is not justified in embarking on anything resembling a trial of the action on conflicting affidavits in order to evaluate the strength of either party's case. Rather, the Court's role is to determine whether the plaintiff raises an arguable case such that it is not plain and obvious that the action will fail [*Bayer Inc v Pharmaceutical Partners of Canada Inc, supra* at para 18, aff'd 2015 FC 797].

[47] Any doubt as to whether a defendant has met its burden on a section 6.08 motion must be resolved in favour of the plaintiff [*Valeant Canada LP v Canada (Health), supra* at para 16].

[48] The parties agree that the test for inducement is three-fold – namely, (i) the act of infringement was or will be completed by the direct infringer; (ii) the completion of the acts of infringement were or will be influenced by the acts of the alleged inducer to the point that, without the influence, direct infringement would not take place; and (iii) the influence must knowingly be exercised by the inducers, that is, the inducer knows that this influence will result in the completion of the act of infringement. As the Federal Court of Appeal has explained, the test for inducement is a difficult one to meet [*Corlac Inc v Weatherford Canada Inc*, 2011 FCA 228 at para 162].

[49] To establish inducement, there must be an underlying factual matrix that can support a legal inference that a third party will actually infringe the claims of the patent. Without such facts, no legal inference of infringement may be drawn. Plausible conjecture is not enough [*Corlac*, *supra* at para 169].

[50] It is well established that there is no infringement of a patent in selling an article which does not in itself infringe the patent even when the vendor knows that the purchaser buys the article for the purpose of using it in the infringement of the patent [*Bayer Inc*, *supra* at para 23].

[51] It is not sufficient for a plaintiff to say that a pharmacist or physician would prescribe KANJINTI in an infringing manner and therefore inducement is made out. It is Amgen's actions which are at issue and not the infringing conduct of others [*Bayer Inc*, *supra* at para 24; *Lundbeck Canada Inc v Ratiopharm Inc*, 2009 FC 1102]. There must be influence by Amgen that must be exercised knowingly and "something more" than simply making the product available is required [*MacLellan v Produits Gilbert Inc*, 2008 FCA 35 at para 38; *Sanofi-Aventis Canada Inc v Laboratoire Riva Inc*, 2008 FC 291 at para 31]. Whether the "something more" consists of inducement, procurement, marketing or some other nexus will depend upon the facts of each particular case [*Aventis Pharma Inc v. Apotex Inc*, 2005 FC 1461].

[52] Infringement by inducement may be established by inferences reasonably drawn from the contents of the product monograph for the generic drug product or evidence related to the dosage form of the generic product or the labelling or marketing of the generic product [*Lundbeck*, *supra* at para 356 and 399]. In *AB Hassle v Genpharm Inc*, 2003 FC 1443 at para 155, Justice Layden-Stevenson held that "subtle references" in a product monograph may be enough to leave the reader with the impression that a drug can be used in a manner that would infringe a patent.

(e) The 596 Patent

[53] The Plaintiffs have not provided the Court with any evidence suggesting direct infringement by Amgen of the 596 Patent. The Plaintiffs' claims appear therefore to rest entirely on allegations of indirect infringement of the 596 Patent by way of inducement.

[54] To successfully prosecute a section 6 action under the *Regulations* in relation to a use patent where indirect infringement is alleged, the Plaintiffs must prove that third parties would, in fact, use the Amgen product for a claimed use in the Plaintiffs' patent and that Amgen had actively induced or encouraged such use.

[55] Amgen asserts that it is plain and obvious that the claim of inducement vis-à-vis the 596 Patent has no chance of success as Amgen has not done "something more" as such term is used in the case law, and that there is no evidence to satisfy the other prongs of the inducement test. Specifically, Amgen asserts that:

A. Something more must be done than simply putting KANJINTI on the market, marketing KANJINTI for the old use (i.e. treating MBC) or failing to expressly advise all potential third parties against using it for the patented use (i.e. in combination with pertuzumab).

B. Any physicians who prescribe KANJINTI in combination with PERJETA will be doing so in furtherance of the current standard of care, not KANJINTI's draft product monograph as the product monograph specifically carves out any reference to PERJETA and reflects the previous standard of care. Amgen simply

seeks to market KANJINTI for the old use and to permit the Plaintiffs to extend their soon-to-be-expired monopoly over the old use would be entirely improper.

C. The Global Documents, and in particular the KANJINTI [redacted] and the [redacted], cannot form the basis of "something more" as they are draft documents that will be modified for use in Canada. Amgen has not yet turned its mind to how it will modify the documents to advise healthcare professionals whether KANJINTI can be used in combination with PERJETA, but it is clear that Amgen's modifications will conform to the approvals provided in its product monograph. As such, these documents cannot be used to argue that Amgen will knowingly attempt to influence a medical oncologist to prescribe KANJINTI in combination with pertuzumab.

D. Ms. O'Quinn has no first-hand knowledge of Amgen's market access plan and based her opinion on the [redacted] assumption that Amgen will seek funding for combination treatment with PERJETA, [redacted]. Moreover, she improperly relies on the Global Documents, notwithstanding Mr. Snowden's caution that it would be incorrect to draw any inferences therefrom.

E. Dr. Amir's evidence that KANJINTI would be prescribed by some medical oncologists for use in combination with PERJETA is simply not enough and even if it were: (i) his evidence is not based on any study or survey of fellow medical oncologists; and (ii) his evidence is undermined by his admission on cross-examination that a key driver of whether oncologists would prescribe KANJINTI in this manner is whether and how it is paid for, and Amgen has confirmed that it

[redacted] Moreover, he also improperly relies on the Global Documents.

[56] The Plaintiffs assert that Amgen has not been silent on inducement and has done "something more" which a trial judge could ultimately consider to be the requisite influence leading to direct infringement by physicians and patients. Moreover, Amgen asserts that it is not plain and obvious that the claim of indirect infringement of the 596 Patent will fail. Specifically, the Plaintiffs assert that:

A. Amgen filed no expert evidence to refute the expert evidence of Dr. Amir and Ms. O'Quinn. The evidence of the Plaintiffs' experts was clear that if KANJINTI is approved with its draft product monograph, it will be funded by public payers for use in combination with pertuzumab and prescribed by oncologists for use with pertuzumab.

B. Dr. Amir's evidence was not undermined on cross-examination. The suggestion that his opinion should be discredited because he did not conduct a survey or study of other oncologists lacks foundation, but in any event is undermined by Amgen's own documentation which clearly demonstrates that oncologists are extremely likely to use a trastuzumab biosimilar in combination with pertuzumab.

C. Ms. O'Quinn's evidence was not undermined on cross-examination. Moreover, Mr. Snowden admitted on cross-examination that [redacted]

[redacted], a public payer may [redacted] fund KANJINTI for use with pertuzumab in MBC.

D. There is a factual dispute between the parties as to whether prescribing KANJINTI with pertuzumab would be an "off-label" use given that Dr. Amir and Ms. O'Quinn opined that KANJINTI in combination with PERJETA could be viewed by medical oncologists and payers as consistent with KANJINTI's overall MBC indication. The Plaintiff asserts that this factual dispute must be determined by the trial judge and demonstrates that the claim is not ripe for dismissal on a section 6.08 motion.

E. The only significant commercial use of trastuzumab in the treatment of MBC is first-line treatment in combination with pertuzumab and a taxane. The Plaintiffs assert that KANJINTI will not be used in MBC as a monotherapy or with a taxane alone, as to do so would be to provide sub-standard care that would be inconsistent with the standard of care implemented after the CLEOPATRA trial. The KANJINTI draft product monograph contains an express reference to [redacted] where it refers to [redacted], which is a sufficient act to satisfy the second prong of the inducement test.

F. Amgen's argument that even if doctors ultimately prescribe KANJINTI in combination with PERJETA, they will only be following the current standard of care and not the draft product monograph is without merit, as a similar argument

was rejected in *Abbott Laboratories Limited v Canada (Ministry of National Health and Welfare)*, 2006 FC 1411.

G. The current drafts of Amgen's Global Documents demonstrate that Amgen plans to answer questions about whether KANJINTI can be used in combination with pertuzumab to treat MBC in a manner that will promote the use of KANJINTI with pertuzumab. While Mr. Snowden's evidence is that these documents still need to be modified for Canadian use, certain responses contained in the Global Documents have already been modified according to jurisdiction [redacted] which casts doubt on Mr. Snowden's evidence. [redacted] As such, the Plaintiffs and the Court cannot know how these documents will ultimately read and the Plaintiffs assert that the Court should draw an adverse inference.

H. The Global Documents demonstrate that Amgen may promote the use of KANJINTI with pertuzumab through an ongoing clinical trial involving KANJINTI and pertuzumab sponsored by [redacted] (the GENPAR-X trial). [redacted], Mr. Snowden admitted on cross-examination that [redacted]

[redacted]

I. The Court should not dismiss this claim given the lack of certainty surrounding the modifications to the Global Documents and in particular, given that the Plaintiffs would then be precluded from commencing an action for infringement in the event that the Global Documents had no meaningful modifications.

J. With respect to the third prong of the inducement test, Amgen is aware, [redacted], that trastuzumab biosimilars will be used in combination with PERJETA and that the only commercially viable use for trastuzumab in MBC is use with PERJETA. The Plaintiffs assert that Amgen's argument that it is seeking to promote KANJINTI for use for the previous standard of care first-line MBC treatment regimen lacks credibility, as that would suggest that Amgen is promoting a sub-standard treatment regime.

K. Amgen's failure to expressly prohibit the combination of KANJINTI with PERJETA grounds an inference that Amgen intends to induce third parties to combine KANJINTI with pertuzumab. While the absence of a disclaimer is not sufficient on its own to satisfy the test for inducement, where there are other indicia of influence like there are here, it should favour a finding of inducement.

[57] The parties have made detailed, contentious submissions as to whether specific principles enunciated in the case law apply based on the facts of this case, whether the assumptions that underpinned the expert evidence of Dr. Amir and Ms. O'Quinn were properly made based on the evidence before the Court and as to the proper interpretation of the documentation placed before the Court on this motion. There are also a number of factual disputes. Having considered the evidence before me and the submissions of the parties (both as detailed above), I am satisfied that it is at least arguable that Amgen has done "something more" within the meaning of the case law that a trial judge could ultimately consider to be the requisite influence leading to direct infringement by physicians and patients. I am also satisfied that the Plaintiffs raise an arguable case in relation to the balance of the test for inducement such that it is not plain and obvious that the claim of indirect infringement of the 596 Patent has no chance of success. Accordingly, Amgen's motion in relation to 596 Patent is dismissed.

(f) The 556 Patent

[58] As was the case with the 596 Patent, the Plaintiffs have not provided the Court with any evidence suggesting direct infringement by Amgen and accordingly, their claims appear therefore to rest entirely on allegations of indirect infringement of the 556 Patent by way of inducement.

[59] Amgen asserts that it is plain and obvious that the claim of inducement vis-à-vis the 556 Patent has no chance of success. Specifically, Amgen asserts that:

A. The Court does not need to engage in claims construction to determine the motion. The meaning of the asserted claims is obvious from a plain reading of the claims – namely, that the asserted claims relate to a new way of identifying

patients who would benefit from HERCEPTIN through IHC and ISH testing, which are two types of well-known testing.

B. In order to be found liable for inducement, the Plaintiffs would have to demonstrate at trial that Amgen told third parties to test patients twice using the specific testing methodologies in the 556 Patent. The Plaintiffs cannot possibly succeed as the KANJINTI draft product monograph does not do so – rather, it tells third parties to test using IHC or ISH.

C. Dr. Amir confirmed on cross-examination that the KANJINTI draft product monograph does not refer to testing using both IHC and ISH or to patients whose tumors score 0 or 1+ using IHC but nevertheless show amplification of the *her2* gene. As such, the draft product monograph cannot form the basis of the Plaintiffs' claims of inducement.

D. In any event, the draft product monograph is irrelevant to the question of inducement, as Dr. Amir confirmed on cross-examination that a pathologist trying to determine what testing to undertaking in relation to a particular patient will not look at the KANJINTI draft product monograph.

E. The Plaintiffs appear to assert that Amgen would not induce infringement of the 556 Patent if it included in the KANJINTI draft product monograph the following statement contained in the 1999 HERCEPTIN product monograph – "N.B. to date, only data derived from immunohistochemistry staining is relevant to treatment with trastuzumab (see PRECAUTIONS – Selection of Patients)".

However, Amgen asserts that that statement is expressly included in section 11.1 of the KANJINTI draft product monograph.

F. The Plaintiffs appear to take issue with marketing KANJINTI to HER2+ breast cancer patients, including patients with IHC 0/1+ ISH+ breast cancer. However, Amgen asserts that that is not what the 556 Patent is about. While the 556 Patent includes those patients, the 556 Patent is about testing. In any event, given the small number of patients that fall within the 556 Patent patient population (estimated at 27 patients in 2017), the risk that KANJINTI will be used to infringe the 556 Patent is extremely low.

[60] The Plaintiffs assert that it is not plain and obvious that its claim of inducement vis-à-vis the 556 Patent has no chance of success. Specifically, the Plaintiffs assert that:

A. There is a live issue between the parties as to the proper construction of the asserted claims of the 556 Patent. Amgen has put forward no evidence as to the proper construction of those claims, but rather is improperly providing a characterization of the invention of the 556 Patent through its legal counsel. There is no evidence before the Court that 556 Patent is restricted to simply the testing of patients in the 556 Patent patient population. On this basis alone, the motion should be dismissed.

B. A proper characterization of the asserted claims of the 556 Patent is that the patent is about treating patients with HERCEPTIN if they fall within a specific patient

population – namely, patients who are IHC 0 or 1+ but nonetheless have *her2* gene amplification.

C. Amgen has effectively admitted on the motion that direct infringement by third parties will occur. The fact that such direct infringement may be in relation to a portion of a very small patient population (27 patients) is irrelevant. Providing treatment to only one patient would be enough.

D. The evidence of Dr. Amir confirms that the KANJINTI draft product monograph and the Global Documents will persuade medical oncologists that KANJINTI is appropriate for all patients in the 556 Patent patient population. The Plaintiffs note that Amgen has filed no evidence to rebut the evidence of Dr. Amir and assert that his evidence was not undermined on cross-examination.

E. The Plaintiffs do not rely solely on the KANJINTI draft product monograph. They also rely on the KANJINTI [redacted]

F. Amgen made the deliberate choice to include a reference to ISH testing in the KANJINTI draft product monograph. Had Amgen included only a reference to IHC like in the 1999 HERCEPTIN product monograph, patients in the 556 Patent patient population would not receive KANJINTI. The Plaintiffs assert that the 1999 HERCEPTIN product monograph, when read in its entirety, actually hurts the position put forth by Amgen. However, Amgen has filed no expert evidence

on the 1999 HERCEPTIN product monograph and therefore to the extent that it is in issue in this proceeding, the Plaintiffs assert that the matter must be left for determination by the trial judge.

G. There is no merit to Amgen's assertion that a pathologist will not review the KANJINTI draft product monograph and therefore the product monograph cannot be the basis for a finding of inducement. Dr. Amir's evidence clearly explained the different roles of medical oncologists and pathologists and he confirmed that medical oncologists will prescribe KANJINTI based on the results of the tests ordered by pathologists. There is clear evidence put forward by the Plaintiffs that the KANJINTI draft product monograph is directed to medical oncologists and clear evidence as to how medical oncologists would interpret the product monograph. As confirmed by Dr. Amir, Amgen expressly defines in the KANJINTI draft product monograph if a tumour overexpresses HER2 using language that a medical oncologist would understand captures the 556 Patent patient population.

H. Amgen cannot seriously contest that it is aware of the 556 Patent, that Amgen is focused on treating the 556 Patent patient population and that Amgen knows that KANJINTI will be used to treat the 556 Patent patient population. Even if Amgen were given the benefit of the doubt, the case law is clear that Amgen cannot turn a blind eye to what it has put in motion.

[61] I am satisfied that there is a debatable issue regarding the proper construction of the asserted claims of the 556 Patent. In such circumstances and based on the evidence before me, I

cannot conclude that it is plain and obvious that the Plaintiffs' claims of inducement vis-à-vis the 556 Patent have no chance of succeeding.

[62] Even if I am wrong and claim construction need not be undertaken, I am satisfied, based on the evidence and arguments detailed above, that the Plaintiffs raise an arguable case in relation to each prong of the test for inducement such that it is not plain and obvious that their claim will fail. Accordingly, Amgen's motion in relation to 556 Patent is dismissed.

Costs

[63] At the hearing of the motion, the parties advised that they had agreed that if one of the parties was entirely successful on the motion, I should order that the successful party is entitled to its costs of the motion fixed in the amount of $25,000.00 payable in any event of the cause. As the Plaintiffs have been entirely successful in resisting this motion, I find that they are entitled to their costs fixed in the amount of $25,000.00 payable in any event of the cause.

THIS COURT ORDERS that:

1. The Defendant's motion is dismissed in its entirety.

2. The Defendant shall pay to the Plaintiffs their costs of this motion fixed in the amount of $25,000.00, inclusive of disbursements and taxes, in any event of the cause.

"Mandy Aylen"

Case Management Judge