Federal Court  Cour fédérale

Date: 20180307

Docket: T-396-13

Citation: 2018 FC 259

BETWEEN:

HOSPIRA HEALTHCARE CORPORATION

Plaintiff

and

THE KENNEDY TRUST FOR RHEUMATOLOGY RESEARCH

Defendant

AND BETWEEN:

THE KENNEDY TRUST FOR RHEUMATOLOGY RESEARCH, JANSSEN BIOTECH, INC., JANSSEN INC. and CILAG GmbH INTERNATIONAL

Plaintiffs by Counterclaim

and

HOSPIRA HEALTHCARE CORPORATION, CELLTRION HEALTHCARE CO. LTD. and CELLTRION, INC.

Defendants to the Counterclaim

REASONS FOR JUDGMENT

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PHELAN J.

I. INTRODUCTION

[1] This trial concerned the validity of Canadian Patent No. 2,261,630 [the 630 Patent] which essentially details the adjunctive use of methotrexate [MTX] and the anti-tumour necrosis factor-α [anti-TNF-α] antibody "infliximab" for the treatment of rheumatoid arthritis [RA] and other autoimmune diseases.

This case also involved a counterclaim that the 630 Patent has been and will be infringed.

[2] RA is an autoimmune disorder that characteristically impacts the joints causing pain and disfigurement, even death.

MTX is a drug that impedes the growth of certain cells.

Infliximab is a chimeric monoclonal antibody biologic drug that prevents TNF-α from binding to TNF-α cell surface receptors. TNF-α is a cytokine (chemical messenger) that plays an important role in the autoimmune reaction.

[3] The Plaintiff in this action is Hospira Healthcare Corporation [Hospira], an interested party under s 60(1) of the *Patent Act*, RSC 1985, c P-4. Hospira markets, uses, and sells the biosimilar infliximab in Canada under the commercial name Inflectra as a treatment for RA.

[4] The Defendant in this action is the Kennedy Trust for Rheumatology Research [Kennedy]. Kennedy holds the 630 Patent, entitled "Anti-TNF Antibodies and Methotrexate in the Treatment of Autoimmune Disease".

[5] In this action, the relief at issue is set out below.

The Plaintiff claimed the following against the Defendant:

(1) a declaration that Canadian Patent 2,261,630 ("the '630 Patent") and each of claims 1-42 are and always have been invalid and of no force and effect, pursuant to s. 60(1) of the *Patent Act* R.S.C., c.P-4, as amended (the "*Patent Act*");

(2) a declaration that the Plaintiff's proposed product will not infringe claims 1-42 of the '630 Patent, pursuant to s. 60(2) of the *Patent Act*;

(3) prejudgment and post-judgment interest;

(4) its costs of this action; and

(5) such further and other relief as this Honourable Court may deem just.

The Defendant (as one of several entities that are Plaintiffs by Counterclaim) claimed the following against the Plaintiff (as one of several entities that are Defendants by Counterclaim):

(a) A declaration that the claims of Canadian Letters Patent No. 2,261,630 (the "630 Patent") are valid and subsisting;

(b) A declaration that the defendants by counterclaim have or will infringe and induce the infringement of claims 1, 2, 3, 5, 6, 9, 10, 12, 15, 17, 18, 19, 21, 22, 25, 26, 28, 31, 33, 37, 38, 39, 40, 41 and 42 of the 630 Patent (the "Asserted Claims") contrary to the *Patent Act*;

(c) An interlocutory and permanent injunction restraining the defendants by counterclaim, by their officers, directors, servants, agents, employees or otherwise, from:

(i) manufacturing, constructing, importing, exporting, selling, offering for sale or using any product that infringes or will be sold for a use that will infringe the Asserted Claims of the 630 Patent; and

(ii) otherwise infringing or inducing the infringement of the Asserted Claims of the 630 Patent;

(d) An order for the delivery-up, or destruction under oath under the supervision of this Court, of all products, in the possession or control of the defendants by counterclaim in infringement of the Asserted Claims of the 630 Patent;

(e) Damages for infringement suffered by Kennedy, Janssen Biotech, Janssen Canada and Cilag in an amount in excess of $50,000, as specified in Rule 182(b) of the *Federal Courts Rules*, exclusive of costs and interest, or an accounting of profits of the defendants by way of counterclaim, whichever the plaintiffs by counterclaim may elect, after due inquiry and full discovery;

(f) Pre-judgment and post-judgment interest on all monetary relief at the rate of 2% above the prevailing Bank of Canada rates;

(g) Costs of and incidental to this action on a solicitor-client basis or such other basis as this Honourable Court may order, plus GST, and including all disbursements;

(h) Such further and other relief this Honourable Court deems just and proper.

II. **FACTUAL BACKGROUND**

A. *GENERAL*

[6] The 630 Patent details the adjunctive use of MTX and infliximab for the treatment of RA and other autoimmune diseases. The history of the 630 Patent is as follows:

1. the patent was filed on August 1, 1997 as PCT GB1997/002058;

2. the patent claims priority from United States Patent Application Serial No. 08/690,775, filed on August 1, 1996;
3. the patent was published on February 12, 1998 as PCT Publication No. 1998/005357;
4. the patent entered the Canadian National Phase on January 25, 1999;
5. the patent was issued on December 4, 2012; and
6. the patent expired on August 1, 2017.

[7] In the early and mid-1990s, existing treatments for RA were sub-optimal with respect to efficacy and/or side effects. There was a pressing need for new and improved treatment options. Researchers discovered a number of pro-inflammatory cytokines in tissue samples from rheumatoid joints, such as interferon, interleukin-1, interleukin-6, TNF-α, and T-cell surface antigens such as CD4 and CD5.

It was hypothesized that the blockade of cytokines or T-cells could be an effective treatment for RA. At this time, biologic treatments were new and held the potential for danger.

[8] Biologics are genetically engineered proteins from human genes and are designed to inhibit specific components of the immune system that play a pivotal role in fueling inflammation.

[9] Researchers pursued a number of therapeutic targets. Drs. Ravinder Maini and Marc Feldmann, the named inventors of the 630 Patent, made the following discovery:

> TNF-α sat at the apex of an inflammatory cascade, and that by blocking TNF-α, one could interfere with the production of other pro-inflammatory cytokines found in rheumatoid joints.

Of the pharmaceutical companies to which they proposed this idea, only Centocor Inc. [Centocor] was interested.

[10] At the time, Centocor (which has since been acquired by Johnson & Johnson) was a small biotech company. It had only one approved drug, Centoxin, a monoclonal antibody treatment for sepsis. It was in the process of developing two biologics: cA2 (infliximab), a chimeric monoclonal anti-TNF-α antibody, as a treatment for sepsis, and cM-T412, a chimeric monoclonal anti-CD4 antibody, as a treatment for RA. A chimeric antibody is one made by combining genetic material from a non-human source, such as a mouse, with genetic material from a human being.

[11] Maini and Feldmann used Centocor's infliximab to design and conduct the T07 trial, a trial wherein ten patients with severe RA were removed from existing treatments ("washed out") and treated with infliximab over the course of eight weeks. The results of this trial were encouraging and the trial was expanded to include a further ten patients; however, the patients all eventually relapsed. Seven patients were treated in an extension study. The results were positive, but there was concern that the duration of effect diminished with repeated infusions – likely as a result of a patient's immune response to therapeutic antibodies through human anti-chimeric antibodies [HACA].

[12] During the T07 trial, Centoxin was withdrawn from the market. This led to Centocor suffering great financial strain as its stock fell 90%. Despite this financial pressure, Centocor supported the T09 trial – a four-week, three-arm, double-blind study.

[13] The T07 and T09 trials established that infliximab could provide patients with rapid and significant relief of RA symptoms; however, the duration of effect proved to be limited. Therefore, Maini and Feldmann designed a further trial – T14 – combining infliximab with MTX. This trial was meant to determine whether the response to infliximab could be maintained long-term and whether the combination was more effective than either infliximab or MTX alone.

[14] The T14 trial was a 26-week, seven-arm, double-blind, dose-finding study covering 101 patients, with 15 patients in each arm of the study. Three arms received infliximab at 1, 3, and 10 mg/kg.

[15] The results of the study established that the combination of MTX and infliximab exhibited enhanced efficacy over either drug alone as well as a sustained duration of effect. The T14, T15, and T17 studies (discussed further below) led to the ATTRACT trial, the Phase III trial which led to the worldwide approval of infliximab for the treatment of RA.

[16] The United States Food and Drug Administration [FDA] approved Remicade (the Defendant's commercial infliximab product) in 1999 for the treatment of RA in combination with MTX. To this day, infliximab is only approved for the treatment of RA in Canada and the United States in combination with MTX.

[17] The allegedly infringing products, Inflectra and Remsima, are subsequent entry biologics containing CT-P13 (an infliximab biosimilar) as the active ingredient. Notices of Compliance were issued by Health Canada in January 2014, following new drug submissions first made by Celltrion Healthcare Co Ltd and Celltrion, Inc [collectively, Celltrion] in 2012. In Canada, Inflectra is imported and distributed by Hospira, following a transfer of Inflectra from Celltrion to Hospira in 2014.

Inflectra has been sold, prescribed, and administered to patients in Canada, including for the treatment of RA. Remsima is not on the market in Canada.

B. *ENTITIES*

[18] A number of entities were involved or implicated in this action:

- **Hospira** is a Canadian pharmaceutical corporation and an interested party under s 60(1) of the *Patent Act*. Hospira manufactures and sells pharmaceutical products including Inflectra, a subsequent entry biologic of Remicade.
- **Celltrion** is a South Korean pharmaceutical group that makes, distributes, markets, and sells biopharmaceutical products. It has a business cooperation agreement with Hospira that covers Inflectra and other biosimilar products.
- **The Kennedy Trust for Rheumatology Research [the Kennedy Trust]** is the owner of the 630 Patent. It is a registered charity and company in the United Kingdom. It was created to serve the needs of researchers investigating the fundamental causes of rheumatic diseases. Kennedy was originally called “the Mathilda and Terence Kennedy Institute of Rheumatology”, became “the Mathilda and Terence Kennedy Institute of Rheumatology Trust” in 2000, and

became the Kennedy Trust in 2012. Whether Kennedy and the Kennedy Trust are the same entity will be discussed below in Issue 1.

- **Janssen Biotech Inc. [Janssen US]** is an American subsidiary of Johnson & Johnson. It is a biotechnology company that manufactures infliximab, which is the ingredient used by Cilag GmbH International to make the Defendant's Remicade.

  Prior to 2011, Janssen US was named Centocor Ortho Biotech Inc. This entity was formed in 2008 following the merger of Centocor and Ortho Biotech Inc. The 1992 research and licensing agreement [1992 Agreement], as amended, allows Janssen US to license the 630 Patent from the Kennedy Trust, which it in turn sub-licenses to Janssen Inc., Cilag GmbH International, and Cilag AG Schaffhausen (Cilag GmbH International's operating company).
- **Janssen Inc. [Janssen Canada]** is the Canadian subsidiary of Johnson & Johnson. It markets Remicade in Canada, which it buys from Cilag. It sub-licenses the 630 Patent from Janssen US.
- **Cilag GmbH International [Cilag]** is a Swiss subsidiary of Johnson & Johnson. It purchases bulk infliximab from Janssen US, which it manufactures into Remicade through its operating company, Cilag AG Schaffhausen. It is a sub-licensee of the 630 Patent.

The Plaintiff and Defendants to the Counterclaim entities are hereafter generally collectively referred to as Hospira. The Defendant and Plaintiffs by Counterclaim will similarly be generally collectively referred to as Kennedy.

C. *630 PATENT EXAMPLES*

[19] Three Examples were disclosed in the 630 Patent, all of which were the subject of considerable evidence in respect of the validity challenge. The Examples were said to support the claims of the 630 Patent.

- **Example 1** [the T14 Study]: A study conducted in Europe between 1994 and 1996, with results published in 1998. In this study, patients who had been using MTX and who had active disease received either MTX, infliximab, or both.
- **Example 2** [the T15 Study]: A study conducted in the United States between 1994 or 1995 and 1995 or 1996 that was randomized, double blinded, and placebo controlled. This study "was intended to evaluate the safety and efficiency of a chimeric monoclonal anti-tumor necrosis factor antibody (cA2) following a single infusion of 5, 10 or 20 mg/kg cA2 in combination with methotrexate".
- **Example 3** [the T17 Study]: An open label study conducted in the United States between 1994 or 1995 and 1995 or 1996. This study "was intended to evaluate the effects of repeated infusions of 10 mg/kg cA2 in combination with methotrexate administered at a dose of 10 mg/week".

D. *WITNESSES*

[20] Hospira called four fact witnesses and five expert witnesses:

a) **Mr. Curtis Bamber** provided testimony on the commercial arrangements between Hospira, Pfizer, Celltrion and other entities (such as wholesaler Innomar and the provincial formularies). In addition, Bamber testified on Inflectra's

similarity to Remicade, the engagement that the Hospira sales team has with prescribing physicians, and the current use of Inflectra in Canada.

b) **Ms. Alla Kron** testified with respect to her engagement with prescribing physicians when promoting Inflectra. She described visits to Dr. Rubin – a later witness.

c) **Dr. Gary Foster** described his (partially unsuccessful) attempts to recreate the tables in the Davis Expert Report and the Pinheiro Report using the data provided in the Pinheiro Report related to data from clinical trials.

d) **Dr. William Schwieterman** provided testimony on his experience with the FDA in the development of drugs and, in particular, the development of biologics.

e) **Dr. Vibeke Strand** is a rheumatologist and a consultant in the pharmaceutical industry. She was qualified as an expert in the treatment of RA with experience in the design, conduct, and evaluation of clinical trials for RA therapies.

Strand provided testimony on the identity of the ordinary skilled worker, the prior art, and the common general knowledge, including the knowledge on treatment of RA, biologic agents, and MTX. She also testified on the design of the Example 1 study, and the insufficiencies of the data provided in support of the Claims of the 630 Patent. In addition, Strand testified that the subject matter of the Claims was previously known based on prior disclosures, and that the invention was obvious in light of the prior disclosures. She also described the promised utilities of the 630 Patent. Finally, Strand provided testimony on the biosimilarity of Remicade and Inflectra.

I found Strand to be a relatively unhelpful and untrustworthy witness. She was impeached multiple times on cross-examination by her testimony in other (related) proceedings. In addition, her close ties to the Plaintiff gave the Court cause for concern. I put little weight on her evidence of prior disclosure which was her principal focus.

f) **Dr. Giovanni (John) Di Battista** was qualified as an expert in antibody structure and function.

Di Battista testified on the difference between CT-P13 (Inflectra) and cA2 (Remicade) in terms of glycosylation. He also described the ordinary skilled worker and the common general knowledge (specifically with respect to glycosylation patterns) during the relevant time period. Di Battista also discussed the importance of minor variations in glycosylation, the meaning of "infliximab", and the comparison between Remicade and Inflectra.

Di Battista was a straightforward, helpful, and credible witness. Nonetheless, I ultimately find that his evidence is insufficient to ground a finding of non-infringement.

g) **Dr. Charles Goldsmith** was qualified as an expert in epidemiology and biostatistics with respect to musculoskeletal diseases such as RA.

Goldsmith provided testimony on the ordinary skilled worker and the biostatistician's approach to analyzing clinical study results. Goldsmith also analyzed the data in the T14 Clinical Study Report and the T14 Maini Article, and concluded that the data was insufficient to support the conclusions drawn. Goldsmith also critiqued the Davis Expert Report.

Goldsmith was not a helpful witness. He did not review the Claims of the 630 Patent, he did not ask to review the raw data, and he did not do his own statistical calculations. There was insufficient basis for accepting his conclusions.

h) **Dr. David Lloyd Scott** is a medical doctor, clinical rheumatologist, researcher, and professor of clinical rheumatology. He was qualified as an expert in the treatment of rheumatology as well as the design, conduct, and evaluation of clinical trials.

Scott testified on the standard practice in the United Kingdom concerning the use of disease modifying anti-rheumatic drugs [DMARDs] as of August 1996, the identity of the ordinary skilled worker, and the use of MTX combination therapy as "the next logical step" in RA treatment. He also testified that it was self-evident that the study described in the ARC 1995 Report would be successful. Scott spoke to a number of his past publications during cross-examination.

i) **Dr. Peter Tugwell** is a medical doctor, clinical rheumatologist, researcher, and professor of medicine and of epidemiology and community medicine. He was qualified as an expert in the treatment of rheumatology, the design, conduct, and evaluation of clinical trials for RA therapies, and musculoskeletal research and the evaluation of evidence with respect to the effectiveness of healthcare interventions for RA.

Tugwell testified as to the next step in biologic development as of August 1, 1996, and the identity of the ordinary skilled worker and the common general knowledge. He testified that the subject matter of the Claims in the 630 Patent

was previously known and obvious, and that the 630 Patent disclosed a method of medical treatment.

Tugwell was highly regarded in his field, and highly experienced. In fact, he was almost too qualified and experienced to give persuasive evidence of what the Person of Ordinary Skill in the Art [POSITA] would know, do, or conclude. Tugwell was a straightforward witness who provided assistance to both the Plaintiff and the Defendant, in almost equal measure.

[21] Kennedy called nine fact witnesses and five expert witnesses:

a) **Dr. Marc Feldmann** is one of two named inventors of the 630 Patent. He testified as to the background and process leading to the invention disclosed in the 630 Patent. He described his relationship with Dr. Ravinder Maini, the other named inventor, and the relationship between Kennedy and the Kennedy Trust. He also described the novelty of the invention, as well as the trials leading to the 630 Patent.

b) **Dr. Thomas Schaible** is a former employee of Centocor and Janssen US. He provided evidence on the development of Remicade from the perspective of someone working at Centocor at the time.

c) **Mr. Pierre Espinasse** is the General Manager of Kennedy. He testified with respect to the history and structure of the Kennedy Trust, as well as the Kennedy Trust's ownership of the 630 Patent.

d) **Mr. Robert Bensen** is the proprietor, President, and CEO of the Charlton Health Group. He provided testimony on the use of Remicade and Inflectra in Charlton Health Group clinics, particularly with respect to MTX combination therapy.

e) **Ms. Lisa Pinheiro** is a vice president at the economic consulting firm Analysis Group. She described the work that she did in transferring data from the appendix of the study report into electronic form, focusing on the data underlying the tables in the 630 Patent.

f) **Mr. Kevin Seeto** is a finance manager at Janssen Canada and responsible for inventory management. In the 2013-2014 period, he was responsible for reporting Canadian Remicade sales to Janssen US by indication as a revenue and strategic planning finance manager. Seeto described the Remicade product and product flow between Cilag, Cilag AG Schaffhausen, Janssen US, and Janssen Canada.

g) **Mr. Graeme Forster** is the finance manager at Johnson & Johnson who is responsible for the calculation and payment of royalties owed under third-party licensing agreements. He testified as to the relationship between Kennedy and Janssen US, including the licences and sublicences for Remicade.

h) **Mr. Jason Nitert** is a business unit director for rheumatology and dermatology with Janssen Canada. He is responsible for the sales and marketing strategy for Remicade. He provided testimony on the Remicade and Inflectra products, as well as promotional efforts and commercial success.

i) **Mr. Glenn Abe** is the director of SEB strategy at Janssen Canada. He testified with respect to IMS data on Inflectra use in Canada, including whether these patients were receiving combination therapy with MTX.

j) **Dr. Michael Schiff** is a medical doctor, clinical rheumatologist, researcher, and professor of medicine and rheumatology. He was qualified as an expert in internal medicine and rheumatology, the development and science of treatments for RA. Schiff identified the POSITA and the state of the art, construed the Claims of the 630 Patent, and provided opinions as to novelty, obviousness, utility, and whether the 630 Patent discloses a method of medical treatment.

In my view, Schiff's description of the POSITA was more realistic than those offered by the bulk of the Plaintiff's experts. His perspective and understanding of the 630 Patent and the circumstances most closely mirrored that of the POSITA identified in the evidence.

k) **Dr. Jack Gauldie** is a biochemist, research immunologist, and professor of immunology. He was qualified as an expert in protein and peptide structures, genetic immunotherapies, cytokines including TNF-α, and antibodies.

Gauldie described the POSITA and testified that CT-P13 is identical to cA2. Gauldie also testified that the differences in glycosylation and additional c-terminal lysine present in CT-P13 played no role in the relevant activity of the antibody.

l) **Dr. Charles Davis** is a biostatistician, a consultant to the pharmaceutical industry, and a professor of biostatistics. He was qualified as an expert in the generation, monitoring, processing, analysis, and interpretation of data from all stages of clinical drug trials. Davis testified as to his analysis of the data on efficacy in the study report and the 630 Patent.

m) **Dr. David Pisetsky** is a medical doctor, immunologist, rheumatologist, researcher, and professor of medicine and immunology. He was qualified as an expert in immunology and rheumatology, the development and science of RA treatments, the analysis and interpretation of clinical trials in the area of rheumatology, cytokines such as TNF-α, and therapeutic antibodies.

Pisetsky provided testimony on the POSITA and the common general knowledge. He also testified that the invention disclosed in the 630 Patent had not been anticipated by any of the prior art references. Most importantly, he testified that it would not have been obvious to engage in combination therapy with MTX, and that the 630 Patent showed utility.

n) **Dr. Laurence Anthony Rubin** is a medical doctor and clinical rheumatologist, as well as a professor of medicine. He was qualified as an expert in rheumatology and immunology, past and present RA treatment in Canada, and the analysis and interpretation of data and the results of clinical drug trials from the perspective of a practising clinical rheumatologist.

Rubin described the POSITA and the common general knowledge. He testified with respect to Remicade and Inflectra, and his own personal practice with Remicade. He also discussed the inventive concept of the 630 Patent (the promise of the 630 Patent, a matter now disposed of by the Supreme Court, which is discussed more fully below) and the Claims of the 630 Patent.

[22] As a general matter, I found that the Defendant's expert witnesses were more balanced, objective, and relevant than those of the Plaintiff. In so saying I want to be clear that in

preferring some experts over others is not an attack on their honesty or trustworthiness. Except with some noted exceptions, these witnesses attempted to be helpful to the Court.

III. **ISSUES**

[23] Kennedy submitted that the issues for the Court to decide are whether or not: (1) Hospira has infringed the Asserted Claims; and (2) the Claims are invalid.

[24] Hospira, on the other hand, argued an astonishing number and veritable panoply of patent law issues, including: ownership of the 630 Patent, the proper parties to claim under the patentee, the claim date for the 630 Patent, the POSITA, the common general knowledge, claim construction, infringement, novelty, inventiveness (including the scope of the applicable prior art and inventive concept), utility (including the promise, demonstration and sound prediction), obviousness-type double patenting, claim ambiguity, whether the claims impermissibly claim a method of medical treatment, overbreadth, and insufficiency.

[25] I see the issues as follows:

Standing Issues

1. Is there any doubt as to the ownership of the 630 Patent?
2. Do Janssen Canada, Janssen US, and Cilag have standing in this action?

Claim Construction

3. Who is the POSITA?
4. What was the common general knowledge at the relevant time?
5. What is the proper claim construction?

Validity of the 630 Patent

6. Is the 630 Patent invalid because it is an unpatentable method of medical treatment?
7. Does the 630 Patent claim improper priority?
8. Is the invention disclosed by the 630 Patent novel (i.e. was the invention anticipated)?
9. Is the 630 Patent invalid for obviousness?
10. Is the 630 Patent invalid due to double patenting?
11. Is the 630 Patent sufficient?
12. Are the Claims of the 630 Patent overbroad?
13. Do the Claims of the 630 Patent exhibit utility?

Infringement

14. Does Inflectra(/Remsima) infringe the Asserted Claims?
15. Did Hospira induce infringement of the 630 Patent?

IV. **ARGUMENT AND ANALYSIS**

A. *STANDING ISSUES*

(1) Issue 1: Ownership of the 630 Patent

[26] Hospira submitted that the Kennedy Trust does not have standing. The evidence showed that the 630 Patent was assigned to Kennedy ("The Kennedy Institute of Rheumatology") by the named inventors.

[27] Firstly, Hospira contended that Feldmann and Maini were not employed by the Kennedy Trust. There was contradiction between Feldman and Espinasse as to whether the inventors were employees of the Kennedy Trust.

[28] Secondly, Hospira said the evidence did not show that "The Kennedy Institute of Rheumatology" was a name used for the Kennedy Trust. In fact, the evidence showed that the Kennedy Trust and Kennedy are two separate entities: the Kennedy Trust has a mandate of support/funding, and Kennedy is a scientific institute. There is no formal relationship between the two, although the Kennedy Trust has supported Kennedy since the mid-1960s.

[29] Finally, Hospira submitted that Kennedy was transferred to Imperial College in 2000, as were the employment contracts of the named inventors. There were also agreements with respect to intellectual property. Following this, Kennedy moved to Oxford University. Kennedy has failed to put any of these transfers or agreements into evidence.

[30] However, the Kennedy Trust submitted that it has gone by a number of informal names and one such informal name was inadvertently used on the Canadian patent filing, among others. This oversight was corrected with the patent office, and subsequent name changes in 2000 and 2012 were similarly recorded. Furthermore, the licensees have been making royalty payments to Kennedy as the owner of the 630 Patent.

[31] In my view, the evidence clearly indicates that Kennedy is the owner of the 630 Patent and any mistake that was initially made on the patent filing was later rectified.

(2) Issue 2: Standing of Janssen Canada, Janssen US, and Cilag in this action

[32] Hospira argued that the burden of establishing standing is on the party claiming standing under s 55(1) of the *Patent Act*. This requires that one have a title or right that can be traced back to the patentee: *Janssen Inc v Teva Canada Limited*, 2016 FC 593 at para 43, 141 CPR (4th) 1 [*Janssen v Teva*] citing *Signalisation de Montréal Inc v Services de Béton Universels Ltée* (1992), [1993] 1 FC 341, 58 FTR 230 (CA) [*Signalisation*].

[33] Hospira further submitted that in this case there is no evidence as to the required title or right traced back from Janssen Canada or Cilag to the purported patentee, Kennedy. Hospira, relying on *Pfizer Canada Inc v Teva Canada Ltd*, 2016 FCA 161, 400 DLR (4th) 723, said that the evidence was inadmissible hearsay.

[34] Hospira further contended that a sublicence cannot exist if the patentee is not aware of the sublicence and does not consent to it, and that this was the case here.

[35] Hospira argued that the royalties are not evidence of the existence of sublicences because they do not relate to the alleged invention – the royalties are not dependant on whether a patient is receiving concomitant MTX, and royalties are also paid on sales of Remicade attributed to psoriatic arthritis, a different indication.

[36] Hospira sought to distinguish this case from *Apotex Inc v Wellcome Foundation Ltd*, [2001] 1 FC 495 at para 99, 186 FTR 274 (CA), aff'd 2002 SCC 77, and *Jay-Lor International*

Inc v Penta Farm Systems Ltd, 2007 FC 358 at para 37, 313 FTR 1 [*Jay-Lor*], on the basis that Kennedy, Janssen US, Janssen Canada, and Cilag are not under common control.

[37] Lastly, on this issue, Hospira submitted that Janssen US and Cilag did not engage in activities for which they would require a licence as their activities do not infringe the 630 Patent. Janssen US does not manufacture or sell infliximab in Canada, nor does the infliximab it manufactures pass through Canada before being transferred to Cilag. Cilag AG Schaffhausen manufactures Remicade outside of Canada and the sale is made to Janssen Canada outside of Canada.

[38] The jurisprudence indicates the following:

a) Any party who, as a user, an assignee, a licensee, or lessee has a title or a right that can be traced back to the patentee, has standing to claim under the patentee (*Signalisation* at para 24).

b) A licensee – exclusive or otherwise, written or unwritten – has standing to claim under the patentee (*Armstrong Cork Ltd Canada v Domco Industries Ltd*, [1982] 1 SCR 907 at 917-20, 136 DLR (3d) 595; *Jay-Lor* at paras 32-38).

c) Where multiple parties each form an integral part of a single supply chain whereby licensed, patented products ultimately find their way to Canada, those parties have standing to claim under the patentee (*Janssen v Teva* at paras 60-68).

[39] In my view, Kennedy has established through admissible evidence that Janssen Canada, Janssen US, and Cilag have standing in this action.

[40] It is not disputed that a licensee has standing to claim under the patentee. The dispute is whether Janssen Canada, Janssen US, and Cilag are licensees – which can be distilled to whether Kennedy has put forward sufficient evidence to show that their titles or rights can be traced back to Kennedy, the patentee.

[41] The evidence indicates that Janssen US is a licensee of the 630 Patent under the 1992 Agreement. Janssen US then granted sublicences to Janssen Canada and Cilag. Hospira's contention that Kennedy was unaware of the sublicences is immaterial. The 1992 Agreement clearly approves of and anticipates the granting of sublicences. It was not necessary for any of the parties to seek express approval for each individual sublicence.

[42] Licences are not required to be in writing (*Janssen v Teva* at para 43). Seeto's evidence, which I accept, was that a written agreement would not be necessary or normal with respect to the related entities of Janssen US and Janssen Canada.

[43] Invoices and purchase orders were put into evidence to demonstrate the flow of infliximab through Janssen US to Cilag, and then of Remicade from Cilag to Janssen Canada. In addition, employees of Janssen Canada and Johnson & Johnson testified as to the existence of sublicences. Both Seeto and Forster indicated that their knowledge of the sublicences derived from conversations with others in the company (in Seeto's case from Forster, and in Forster's case from the legal department).

On this aspect, Hospira argued that it is hearsay.

[44] Recently, in *R v Bradshaw*, 2017 SCC 35, [2017] 1 SCR 865 [*Bradshaw*], the Supreme Court reviewed the rule against hearsay and the principled exceptions to the hearsay rule. Although the Supreme Court indicated that there was real danger in the acceptance of hearsay evidence, it noted that accurate fact finding may in fact be impeded in some instances by the exclusion of hearsay evidence. Under the principled approach to hearsay that has developed in the jurisprudence, hearsay may be admitted into evidence if it is both necessary and sufficiently reliable (*Bradshaw* at para 18).

[45] In my opinion, this evidence is not necessary. The invoices and purchase orders establish that the companies are working in concert to make Remicade available in Canada.

[46] The 1992 Agreement establishes that Janssen US has the right and ability to grant sublicences. Although they are arguably not under common control as was the case in *Jay-Lor*, the parties in this case have indeed "structured their affairs in a manner consistent with a licensee-licensor relationship" (*Jay-Lor* at para 37). In addition, no other licence has been granted to a third party.

[47] In my view, common control is not a required element for tracing interest under a patent – it is simply one factor that may be persuasive.

[48] Therefore, I find that it is a reasonable inference, based on the evidence and the facts, that Janssen US, Janssen Canada, and Cilag had licences/sublicences for the invention disclosed by

the 630 Patent. As per *R v Munoz* (2006), 86 OR (3d) 134, 205 CCC (3d) 70 at paras 23-31 (Sup Ct J), the Court is entitled to draw reasonable inferences.

[49] Further, with respect to the royalties, Hospira may be correct that the evidence put forward fails to establish the exact amount of royalties related to the use of Remicade for concomitant treatment with MTX in MTX incomplete responders.

[50] However, in my view, the evidence is sufficient to show that some amounts of royalties were paid for this use. It is not necessary at this time to determine the precise amount of royalties paid. The evidence of payments is consistent with the other evidence of the existence of sublicences.

[51] Moreover, if the evidence of Seeto and/or Forster is necessary, then the Court must determine if it is reliable: "threshold reliability can be established by showing that (1) there are adequate substitutes for testing truth and accuracy (procedural reliability) or (2) there are sufficient circumstantial or evidentiary guarantees that the statement is inherently trustworthy (substantive reliability)" (*Bradshaw* at para 27).

[52] In my view, substantive reliability has greater relevance in the instant case – one must "consider the circumstances in which it was made and evidence (if any) that corroborates or conflicts with the statement" (*Bradshaw* at para 30). The threshold for reliability is high, but it does not require certainty.

[53] In *Bradshaw*, the Supreme Court considered when corroborative evidence may be relevant to a finding of substantive reliability:

> [44] In my view, the rationale for the rule against hearsay and the jurisprudence of this Court make clear that not all evidence that corroborates the declarant's credibility, the accused's guilt, or one party's theory of the case, is of assistance in assessing threshold reliability. **A trial judge can only rely on corroborative evidence to establish threshold reliability if it shows, when considered as a whole and in the circumstances of the case, that the only likely explanation for the hearsay statement is the declarant's truthfulness about, or the accuracy of, the material aspects of the statement.** If the hearsay dangers relate to the declarant's sincerity, truthfulness will be the issue. If the hearsay danger is memory, narration, or perception, accuracy will be the issue.
>
> [45] First, corroborative evidence must go to the truthfulness or accuracy of the *material aspects* of the hearsay statement (see *Couture*, at paras. 83-84; *Blackman*, at para. 57). **Hearsay is tendered for the truth of its contents and corroborative evidence must go to the truthfulness or accuracy of the content of the hearsay statement that the moving party seeks to rely on.** Because threshold reliability is about admissibility of evidence, the focus must be on the aspect of the statement that is tendered for its truth. The function of corroborative evidence at the threshold reliability stage is to mitigate the need for cross-examination, not generally, but *on the point* that the hearsay is tendered to prove.
>
> …
>
> [47] Second, at the threshold reliability stage, corroborative evidence must work in conjunction with the circumstances to overcome the *specific hearsay dangers* raised by the tendered statement. When assessing the admissibility of hearsay evidence, "the scope of the inquiry must be tailored to the particular dangers presented by the evidence and limited to determining the evidentiary question of admissibility" (*Khelawon*, at para. 4). Thus, to overcome the hearsay dangers and establish substantive reliability, corroborative evidence must show that the material aspects of the statement are unlikely to change under cross-examination (*Khelawon*, at para. 107; *Smith*, at p. 937). **Corroborative evidence does so if its combined effect, when considered in the circumstances of the case, shows that the *only likely explanation* for the hearsay statement is the declarant's truthfulness about, or the accuracy of, the material aspects of the statement** (see *U. (F.J.)*, at para. 40). Otherwise, alternative

> explanations for the statement that could have been elicited or probed through cross-examination, and the hearsay dangers, persist.
>
> [Emphasis added; italics in original; footnotes omitted.]

[54] A trial judge is directed to consider alternate or speculative explanations for the corroborative evidence (*Bradshaw* at para 48). The Supreme Court summarized the proper approach as follows:

> [57] In sum, to determine whether corroborative evidence is of assistance in the substantive reliability inquiry, a trial judge should
>
> 1. identify the material aspects of the hearsay statement that are tendered for their truth;
>
> 2. identify the specific hearsay dangers raised by those aspects of statement in the particular circumstances of the case;
>
> 3. based on the circumstances and these dangers, consider alternative, even speculative, explanations for the statement; and
>
> 4. determine whether, given the circumstances of the case, the corroborative evidence led at the *voir dire* rules out these alternative explanations such that the only remaining likely explanation for the statement is the declarant's truthfulness about, or the accuracy of, the material aspects of the statement.

[55] In my view, the corroborative evidence in this case (discussed above with respect to the necessity of this evidence) confirms the threshold reliability of the evidence. The evidence tends to establish the accuracy of the material aspects of the hearsay statements (i.e., that the interested parties had licences) and its combined effect indicates that the only likely explanation is the accuracy of the hearsay statements.

[56] The specific hearsay dangers at play in this case include the accuracy of the statements, as they were not recorded – however, Seeto's reliance on Forster's evidence is relatively unproblematic, as Forster was available for cross-examination. It is Forster's reliance on information supplied by the legal team that holds greater danger in terms of specific hearsay dangers. There is no alternative or speculative explanation that explains the actions of these parties other than the grant of sublicences for the purposes of acting in concert to create and distribute a commercially viable product.

[57] Finally, I reject Hospira's contention that Janssen US and Cilag would not require licences. As discussed further below with respect to infringement, guidance from *Saccharin Corp Ltd v Anglo-Continental Chemical Works, Ltd* (1900), 17 RPC 307 (Ch (Eng)) [*Saccharin*], indicates that these entities would require licences.

B. *CLAIM CONSTRUCTION*

(1) Issue 3: Who is the POSITA?

[58] There was considerable agreement among the experts as to the basic qualifications of a POSITA. It would be a practicing rheumatologist or clinical immunologist with (i) a medical degree and further training in this field; (ii) an interest in new treatments for RA patients; (iii) an understanding of RA clinical outcome measures; and (iv) some experience interpreting published clinical trial results.

[59] Some of the experts agreed that portions of the 630 Patent are directed at a post doctorate level molecular biologist or a biochemist who had experience with monoclonal antibodies. However, other experts were of the view that this qualification was not necessary.

[60] Hospira added that the POSITA can be a team of persons with the necessary knowledge and experience for the problem at hand, and the skill set of the POSITA should resemble, to some extent, the skills used to solve the problem addressed by the patent. Further, the POSITA is able to consult with persons possessing other skill sets. Hospira cited the Court's decision in *Bayer AG v Novopharm Ltd*, 2006 FC 379, 289 FTR 263 [*Bayer v Novopharm*] for support:

> [47] Bayer contends that such a person, particularly in respect of the '006 patent, is a multi-disciplinary amalgam of skilled people with the skills of a formulator and clinician. The POSITA bears some resemblance to the team of skills used to solve the '547 patent problem. The following quote from *Bayer Aktiengesellschaft v. Apotex Inc.* (1995), 60 C.P.R. (3d) 58 at 79 is supportive of Bayer's position:
>
> > The notional skilled technician can be a composite of scientists, researchers and technicians bringing their combined expertise to bear on the problem at hand: "This is particularly true where the invention relates to a science or art that transcends several scientific disciplines." (Per Wetston J. in *Mobil Oil Corp. v. Hercules Canada Inc.* (unreported, September 21, 1994, F.C.T.D., at p. 5 [now reported 57 C.P.R. (3d) 488 at p. 494, 82 F.T.R. 211].)
>
> [48] Novopharm, on the other hand, contends that the POSITA is a formulator with no background or experience in clinical matters. In respect of obviousness double-patenting, Novopharm relies on the Federal Court of Appeal's judgment in *Beloit Canada Ltd. v. Valmet Oy* (1986), 8 C.P.R. (3d) 289 (FCA) at 294:
>
> > The test for obviousness is not to ask what competent inventors did or would have done to solve the problem. Inventors are by definition inventive. The classical touchstone for obviousness is the technician skilled in the art but having no

> scintilla of inventiveness or imagination; a paragon of deduction and dexterity, wholly devoid of intuition; a triumph of the left hemisphere over the right. The question to be asked is whether this mythical creature (the man in the Clapham omnibus of patent law) would, in the light of the state of the art and of common general knowledge as at the claimed date of invention, have come directly and without difficulty to the solution taught by the patent. It is a very difficult test to satisfy.
>
> [49] Novopharm's position, however, is undermined by its witness' (Dr. Lachman) evidence at Questions 66-77, to the effect that some outside input is necessary for the formulator to do his/her job. **The scientific equivalent of the "reasonable person" is not so devoid of outside knowledge or the need for consultation as the above quote from Beloit is said to indicate. Therefore, Bayer's description of the relevant POSITA is more consistent with the realities of these circumstances.**
>
> [Emphasis added.]

[61] Hospira further added that the 630 Patent is addressed to a person who could make the anti-TNF-α antibody. The 630 Patent describes antibody production in great detail and Hospira's experts agreed that the POSITA would have knowledge of the manufacture of the antibody. Further, Gauldie agreed that the POSITA would include someone with knowledge of protein chemistry, and Kennedy's other experts agreed in their initial reports that the POSITA would have knowledge of antibodies and antibody production – although they later resiled from this position.

[62] Hospira contended that the Kennedy experts based their views on the "fundamentally" erroneous view that the POSITA could not access or make the antibody, formulate the antibody, or use an unapproved product. This is problematic because the jurisprudence does not require that a drug be approved or on the market before it can be found to be anticipated or obvious.

[63] Hospira submitted that all of the experts attributed knowledge of clinical trials or trial design to the POSITA (which would be gleaned from reviewing the literature). The experts disagreed as to the POSITA's experience in the design of clinical trials. For example, Tugwell indicated that the POSITA would have experience in drafting protocols for clinical trials, while Schiff and Rubin indicated that the POSITA would not do this and would also not have the requisite infrastructure for clinical trials.

[64] Hospira suggested that the evidence of Kennedy's experts was inconsistent and changed over the course of the proceedings. For example, Hospira indicated that experts such as Rubin and Schiff initially indicated that the POSITA would have knowledge of or experience with the design and interpretation of clinical trials, but that they later changed their positions.

Further, as noted above, the Kennedy experts did not take into account that the POSITA is able to consult with someone with the necessary skill set.

[65] There was also significant disagreement between the parties on whether the POSITA would have experience with or be a biostatistician – a position favoured by Hospira.

[66] The 630 Patent references statistical measures such as statistical significance and p-values, which would have been determined by biostatisticians. Hospira submitted that Maini and Feldmann relied on a biostatistician at Centocor to design and interpret Example 1. The reality of the development of the invention, then, is said to involve a biostatistician on the POSITA team, or consultation with a biostatistician.

[67] Certainly Kennedy's experts admitted that biostatisticians would help with the design of clinical trials and the analysis and interpretation of the results. The disagreement was, to some extent, as to what degree of involvement was required.

[68] Kennedy contended that Hospira overqualified the POSITA, which is improper (see e.g. *Jay-Lor* at para 87):

- Strand indicated that the POSITA included a regulator. Further, she stated that the POSITA wrote academic literature.
- Tugwell indicated the POSITA needed the skills required to run clinical trials of experimental biologics (but admitted that about 40 groups in the Western world did so in 1996).
- Di Battista testified that the POSITA was a biostatistician, because this skill set would be required to develop a drug commercially, a matter not in his Expert Report.
- Goldsmith indicated that the POSITA included a biostatistician, but also admitted that he (a biostatistician) did not read the Claims of the 630 Patent as they were not his area.

[69] Kennedy submitted that the qualifications put forward by Hospira are excessive. The POSITA is "neither first nor last in her class but somewhere in the middle" (*Merck-Frosst-Schering Pharma GP v Canada (Health)*, 2010 FC 933 at para 69, 385 FTR 1 [*Merck-Frosst-Schering*]; see also *Amgen Canada Inc v Apotex Inc*, 2015 FC 1261 at para 45, 138 CPR (4th) 383, appeal dismissed 2016 FCA 196 [*Amgen*]).

[70] Kennedy also submitted that the POSITA "spent the vast majority of his or her time (80-90%) seeing patients in the clinic, and spent the remainder staying up to date on the relevant literature, intermittently attending annual meetings, and from time-to-time enrolling patients in trials and performing the necessary evaluations". This is not a biostatistician, a regulator, or a rheumatologist designing and running clinical trials.

[71] So despite what would have appeared to be significant agreement as to the core expertise of the POSITA, it was the ancillary skills and the practical realities which were in dispute.

[72] The Court is mindful that in *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at para 53, [2000] 2 SCR 1067, the Supreme Court stated that "the patent specification is not addressed to grammarians, etymologists or to the public generally, but to skilled individuals sufficiently versed in the art to which the patent relates to enable them on a technical level to appreciate the nature and description of the invention".

[73] In *Free World Trust v Électro Santé Inc*, 2000 SCC 66, [2000] 2 SCR 1024 [*Free World Trust*], the Supreme Court stated:

> 44 The courts have traditionally protected a patentee from the effects of excessive literalism. The patent is not addressed to an ordinary member of the public, but to a worker skilled in the art described by Dr. Fox as
>
> > a hypothetical person possessing the ordinary skill and knowledge of the particular art to which the invention relates, and a mind willing to understand a specification that is addressed to him. **This hypothetical person has sometimes been equated with the "reasonable man" used as a standard in negligence cases.** He is assumed to be a man who

> is going to try to achieve success and not one who is looking for difficulties or seeking failure.
>
> (Fox, *supra*, at p. 184)
>
> It is the "common knowledge" shared by competent "ordinary workers" that is brought to bear on the interpretation: Fox, *supra*, at p. 204; *Terrell on the Law of Patents* (15th ed. 2000), at p. 125; I. Goldsmith, *Patents of Invention* (1981), at p. 116.
>
> [Emphasis added.]

[74] As noted earlier, in *Merck-Frosst-Schering* at para 69, this Court described this person as "neither first nor last in her class but somewhere in the middle". The POSITA is not the gold medallist and is not exceptional. The POSITA may be an "amalgam" or team of people with different skills (*Bayer v Novopharm* at paras 47-49). In addition, the POSITA may, properly, consult with others.

[75] Hospira overinflated the POSITA profile. In my view, the POSITA would not include a biostatistician, regulator, or someone with experience drafting clinical trial protocols. These elements would significantly overpower or overqualify the POSITA, turning the POSITA into an expert rather than an ordinary skilled worker. As Hughes J stated in *Amgen* at para 45, "a POSITA is a person of ordinary skill in the art, not the newcomer, not the greatest of experts, but an ordinary person in the field at issue" [underlining in original].

[76] Hospira's experts, at times, imbued the POSITA with truly extraordinary levels of skill and experience, in line with the greatest of experts working on the cutting edge of development.

[77] Although the 630 Patent contained biostatistics, these were not essential to the Claims of the 630 Patent. This was confirmed by Hospira's expert biostatistician Goldsmith, who indicated that the Claims were not his area of expertise.

[78] Similarly, the POSITA would not be or include a regulator – and, in fact, a regulator was not involved in the development of the invention.

[79] Further, although the POSITA would have some knowledge and experience of clinical trials, it is the exceptional rheumatologist rather than the ordinary rheumatologist who would be drafting protocols for clinical trials.

[80] Therefore, as put forward by Kennedy's experts, I have concluded that the POSITA was a rheumatologist or team who treated patients, was up-to-date with the literature, sometimes attended meetings, and could have some involvement in clinical trials (i.e., enrolling patients or performing evaluations). Given the Claims of the 630 Patent, the POSITA or team may include a post-doctorate level molecular biologist or a biochemist with experience with monoclonal antibodies.

(2) Issue 4: What was the common general knowledge at the relevant time?

[81] The relevant date for assessing the common general knowledge of the POSITA is the claim date of August 1, 1996 (*Pollard Banknote Limited v BABN Technologies Corp*, 2016 FC 883 at para 153, 141 CPR (4^{th}) 329).

[82] This is one of the hotly contested issues in this litigation. Hospira placed considerable importance on this issue and tied it to its position on novelty and obviousness.

(a) *Re: MTX*

[83] Hospira's position was that as of the relevant date, RA treatment largely consisted of DMARD therapy (MTX, sulfasalazine, gold salts, and hydroxychloroquine) and the use of NSAIDs and steroids. It contended that the experts agreed that MTX was used for the majority of patients and was the "gold standard" therapy.

Further, Hospira contended that MTX was known to be an immunosuppressive or to have immunosuppressive properties in the context of RA treatment.

[84] Hospira contended that the main patient population in need of treatment at this time were MTX incomplete responders (that is, those patients receiving MTX but whose disease was not completely controlled by MTX).

[85] However, as pointed out by Kennedy, the underlying mechanisms of RA were unknown in the 1990s and clinical remission was rare. Some patients were "nonresponders" who did not improve with treatment by DMARDs such as sulfasalazine, MTX, hydroxychloroquine, and gold salts, while other patients achieved limited results.

By 1996, there had been no significant advances in RA treatment for a number of years.

[86] MTX was a well-known treatment for RA in the mid-1990s, albeit reserved for serious cases. Even today the exact mechanism of action of MTX in RA is unknown, although the

experts agreed that the mechanism of action is multifactorial. A number of mechanisms of action had been proposed in the mid-1990s, and Pisetsky suggested that MTX is best described as an anti-inflammatory when used for RA treatment.

[87] MTX was not considered to be a traditional immunosuppressive, unlike azathioprine, hydroxychloroquine, and cyclosporine. Kennedy argued that MTX "did not cause opportunistic infections (as do traditional immunosuppressives), was not used in any setting where traditional immunosuppressives were used (such as organ transplantation), and was not designated a traditional immunosuppressive drug in the standard pharmacology reference textbooks (including the Compendium of Pharmaceuticals and Specialties)".

[88] A further complicating factor cited by Kennedy was that in the 1990s biologics were unproven.

[89] A number of targets and agents were being tried in the 1990s, focusing on interference with CD4+ and other T-cells (white blood cells which were believed to stimulate production of pro-inflammatory cytokines). Cytokines themselves were also a target, although a less popular one. Kennedy submitted that the way forward at this point was not clear. Potential drugs included CD5-ricin immunoconjugate [CD5-IC], CAMPATH-1H, anti-CD4 antibodies, IL-1 and IL-2, CTLA4Ig, IL1-RA, TNF antibodies and soluble receptors, ICAM-1, and oral collagen. The success rate was alleged to be low.

[90] Almost all of the numerous agents tried had failed due to lack of efficacy and/or the presence of intolerable side effects. For example, cM-T412 (an anti-CD4+ antibody) and CAMPATH-1H (a CD52 antibody) both failed due to the presence of serious side effects.

[91] Kennedy argued that the POSITA would have been aware that these treatments were discontinued by August 1996. Other once-promising treatments such as anti-CD5-IC and a chimeric anti-CD7 antibody also failed.

Further, the potential for HACA responses complicated development.

(b) *Re: Combination Therapy with MTX*

[92] A critical issue is the point at which combination therapy with MTX was accepted as a proper therapy.

[93] Hospira argued that combination therapy involving NSAIDs, DMARDs, and steroids was the "backbone" of rheumatology practice by 1994. Hospira's expert Schiff suggested that the POSITA was even using combinations that had not been established as safe or effective through randomized controlled trials.

MTX was heavily utilized in combination therapies, and many MTX incomplete responders were treated with additional DMARDs.

[94] Hospira cited several trials involving combination therapy with MTX:

- Cyclosporine and MTX: After cyclosporine was found to be effective as a monotherapy, trials of combination therapy with MTX or gold incomplete

responders were the next step. The results were clinically and statistically significant.

- Triple Therapy: A trial was conducted involving triple therapy of MTX, hyproxychloroquine, and sulfasalazine, which was found to be more effective than MTX alone.

[95] Hospira also relied on the Elliott studies as part of the common general knowledge. Further, some of the experts agreed that the most promising biologics were anti-TNF-α agents.

[96] However, Kennedy asserted that combination therapy was not popular in 1996, that no biologics had yet been approved so only combinations of DMARDs were available, and that there was no consensus that a combination of DMARDs was more beneficial than MTX alone.

[97] Kennedy relied on such evidence as the Felson Meta-Analysis, leading research at the time, which concluded that "[c]ombination therapy, as it has been used in recent clinical trials, does not offer a substantial improvement in efficacy, but does have higher toxicity than single drug therapy". Similar conclusions and concerns were echoed by other researchers.

Although combination therapy with cyclosporine and MTX suggested improved outcomes, this combination remains rarely used even today.

[98] Triple therapy was only rarely used. Kennedy submitted that combination therapy was far from routine during this period.

[99] Kennedy argued that POSITAs viewed DMARD combination therapy as "risky and unproven". One survey study published in 1995 indicated that only 17% of patients were being treated with combination therapy. Another study, published more recently and co-authored by Scott, indicated that only one patient out of two hundred had received combination therapy in 1996. This study looked at real-world patient chart data, which is more reliable than survey data.

[100] Kennedy submitted that combinations with biologics would not have been popular because they were unproven and largely untested. Further, experts for both Kennedy and Hospira agreed that the "holy grail" of drug development was targeted monotherapy.

[101] As noted above, there was concern with respect to HACA responses limiting long-term use of biologics. Kennedy submitted that combination therapy was "far from an established solution" to this problem. I have concluded that by 1996, both biologics that had been tried in combination with MTX had failed (an anti-CD4+ antibody and anti-CD5-IC).

[102] New therapeutic agents were typically conducted under "washout" conditions, meaning that patients were withdrawn from DMARD therapy prior to the trial. This was done with etanercept and adalimumab – later trials included combination therapy with MTX, but these were published well after monotherapy trials.

[103] Kennedy argued that by 1998, the utility of combination therapy was still unclear.

[104] The evidence showed that the experts, apart from Strand, agreed that the outcome of a clinical trial for a novel RA therapy could not be predicted in advance. A number of biological interventions had failed.

[105] The evidence also established that the experience with corticosteroids had a lasting impression with respect to thinking about biologic agents. Corticosteroids were discovered in pregnant women, who often went into remission during pregnancy. Although patients showed profound improvements, there were side effects and toxicities associated with long-term treatment.

[106] Against this background of the competing perspectives on the common general knowledge, it is necessary to return to first principles.

[107] The common general knowledge is that which is generally known by the POSITA at the relevant time. In *Mylan Pharmaceuticals ULC v Eli Lilly Canada Inc*, 2016 FCA 119, [2017] 2 FCR 280 [*Mylan v Eli Lilly*], the Federal Court of Appeal addressed the distinction between prior art and the common general knowledge:

> [23] Prior art is the collection of learning in the field of the patent at issue. It comprises any publically available teaching, however obscure or not generally accepted.
>
> [24] The common general knowledge, in contrast, is the "knowledge generally known by persons skilled in the relevant art [skilled persons] at the relevant time": *Apotex Inc. v. Sanofi-Synthelabo Canada Inc.*, 2008 SCC 61, at para. 37, [2008] 3 S.C.R. 265. Unlike the prior art, which is a broad category encompassing all previously disclosed information in the field, a piece of information only migrates into the common general knowledge if a skilled person would become aware of it and accept it as "a good basis for further action": *General Tire & Rubber Co.*

> *v. Firestone Tyre & Rubber Co.*, [1971] F.S.R. 417, (1972) R.P.C. 457 at 483 (C.A.).

[108] The common general knowledge is "derived from a commonsense approach to the practical question of what would in fact be known to an appropriately skilled addressee — the sort of man [*sic*], good at his job, that could be found in real life" (*General Tire & Rubber Co v Firestone Tyre & Rubber Co*, [1972] RPC 457 (HL (Eng)), cited in *Eli Lilly and Company v Apotex Inc*, 2009 FC 991 at para 97, 351 FTR 1).

[109] Although the parties appear, at first glance, to have wildly diverging views on the common general knowledge, in fact there is a great deal of overlap between their positions. For example, the parties agree that MTX was a DMARD commonly used for MTX treatment – they simply disagree as to the extent that it was used (i.e., whether it was the "gold standard" for treatment). The parties also agree that MTX has immunosuppressive properties – they simply disagree as to whether it is a "traditional immunosuppressive drug".

[110] With respect to MTX, the parties agree that it was a well-known treatment for RA in the 1990s. The Matzel Survey published in 1998, "How Canadian and US Rheumatologists Treat Moderate or Aggressive Rheumatoid Arthritis: A Survey", indicated that when faced with aggressive RA, 68.7% of Canadian rheumatologists would consider MTX their first choice drug.

[111] In my view, the literature and the expert evidence clearly established that MTX was a popular treatment option for severe RA and that it was one of the more popular, if not the most popular, DMARD for treating severe RA.

[112] Further, the vast majority of the experts agreed that MTX was known to have immunosuppressive properties. However, it was unanimous that the mechanism of action for MTX was (and remains) unknown.

[113] In terms of anti-TNF-α and other biologics, the efficacy of infliximab was part of the common general knowledge due to the publication of the Elliott studies in 1994 and 1995. Elliott 1994 disclosed the results of the T07 trial, and Elliott 1995 was a review article outlining Kennedy's work with infliximab. The concern with respect to HACA responses was also part of the common general knowledge.

[114] However, that being said, a relatively large number of biologics were being tested in the 1990s, including anti-CD4 antibodies, CAMPATH 1H, CD5-ricin immunoconjugate, ICAM-1, and oral collagen, among others. Some of these biologics had failed as of August 1996, including cM-T412 (an anti-CD4+ antibody) and CAMPATH-1H (a CD52 antibody). There was no certainty or even expectation of certainty with respect to the use of biologics.

[115] The literature of the time does not disclose a consensus with respect to the benefit of combination therapy. It is undeniable that some combinations of DMARDs and of biologics and DMARDs were being studied and/or discussed as outlined below:

a) In 1994, the Felson Meta-Analysis (an analysis of the available studies) concluded that combination therapy with DMARDs did not offer substantial improvement in efficacy and was associated with more toxicity than monotherapy.

b) In 1995, Tugwell et al published a study of combination therapy with cyclosporine and MTX (both DMARDs) in severe RA. This article indicated that monotherapy, due to its lack of efficacy, was being reconsidered in favour of combination therapy. It also indicated that many rheumatologists considered MTX to be their "drug of choice". The study found that "[p]atients with rheumatoid arthritis who had only partial responses to methotrexate had clinically important improvement when cyclosporine was added to their treatment". The article expressed some concerns with respect to the long-term risk of cancer.

c) In May of 1996, O'Dell et al published a study comparing treatment with MTX alone, the combination of sulfasalazine and hydroxychloroquine, and a combination of all three medications (all DMARDs). This article noted that the responses of patients to monotherapy were often "suboptimal". It further indicated that many patients are treated with combinations of DMARDs. As in Tugwell et al, it also indicated that many rheumatologists considered MTX to be their "drug of choice". The study concluded that the triple combination therapy was more effective than treatment with MTX alone or with the combination of sulfasalazine and hydroxychloroquine.

d) In June of 1996, Bologna and Sany published an article on combination regimes for RA. It indicated that combining drugs was known to be effective, although there was no evidence of long-term effects. It stated that "there are still several combinations to be studied including methotrexate with 'targeted' drugs such as anti-CD4 and anti- TNF-α antibodies or the soluble TNF-α receptor".

Therefore, the decision was made by the sponsoring pharmaceutical company and the FDA to have the first study with cM-T412 in a cohort of patients with RA who were taking stable doses of MTX. The article acknowledged that potential disadvantages included unknown toxicities and lack of evaluation of efficacy.

e) In July of 1996, Moreland published a study titled "Initial Experience Combining Methotrexate with Biologic Agents for Treating Rheumatoid Arthritis". This study concerned the combination of an anti-CD4 monoclonal antibody, cM-T412, with MTX. The study was designed as a combination study because "[w]ith the initial trials evaluating an agent never previously used as a therapy for RA, it was felt that treatment with cM-T412 for 6 months as the only therapeutic agent would not be appropriate."

As part of the "Future Considerations" section of this article, Moreland stated as follows:

> With emerging positive clinical results using chimeric and humanized anti-TNF Mab as well as recombinant soluble TNF receptor fusion proteins, we now have the opportunity to combine these TNF inhibitors with MTX, or perhaps other DMARD. However, we should proceed with caution for potential serious adverse events, including opportunistic infections and malignancy, when combining MTX and an inhibitor of TNF.

[116] In summary and without limiting the above, the Court concludes the following in respect of the common general knowledge:

a) Throughout much of the 1990s, the underlying mechanisms of RA were unknown, as was the mechanism of MTX.

b) MTX was not considered to be a traditional immunosuppressive drug.

c) Biologics were unproven and there was no clear path of research.

d) There was no direction of research since the list of drugs in issue was long and the success rate for positive results was low.

e) In 1996, combination therapy with DMARDs was not common and often viewed as risky and uncertain.

f) The risk and uncertainty for combinations of DMARDs with biologics was even greater. Monotherapy was the common direction.

g) MTX was viewed as potentially interfering with the action of TNF-α – the antibody in the 630 Patent. An even more negative view was taken of combining two therapies with overlapping mechanisms of action.

h) The weight of the evidence, Strand notwithstanding, was that it was impossible to predict the outcome of a clinical trial of a novel therapy in RA, especially until attempted in humans.

[117] The common general knowledge, as described, pointed away from what was claimed in the 630 Patent.

(3) Issue 5: What is the proper claim construction?

[118] There is no significant disagreement between the parties with respect to the principles of claim construction. These were well summarized by Mactavish J in *Lundbeck Canada Inc v Ratiopharm Inc*, 2009 FC 1102 at paras 39-63, 357 FTR 75 as follows:

> [26] Before examining the issues raised by the parties in relation to questions of validity and infringement, the Court must construe the patents in issue. The Court is to determine objectively, through

> the eyes of the person skilled in the art, what such a person would have understood the inventor or inventors to mean as of the relevant date: see *Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, [2000] 2 S.C.R. 1067, at paras. 45, 53.
>
> [27] The claims of a patent are to be construed purposively, having regard to the intentions of the inventors as derived from the patent and with reference to the entire specification. A court should construe a patent with a judicial anxiety to support a useful invention: see *Whirlpool* at paras. 42-50; *Free World Trust v. Électro Santé Inc.*, 2000 SCC 66, [2000] 2 S.C.R. 1024; *Consolboard Inc. v. MacMillan Bloedel Saskatchewan Ltd.*, [1981] 1 S.C.R. 504, 56 C.P.R. (2d) 145 at 157.
>
> [28] Expert assistance may be provided with respect to the meaning of certain terms, as well as the knowledge that a person skilled in the art would have had as of the relevant date: see *Janssen-Ortho Inc. v. Novopharm Ltd.*, 2007 FCA 217, 59 C.P.R. (4th) 116, at para. 4; *Halford v. Seed Hawk Inc.*, 2006 FCA 275, 54 C.P.R. (4th) 130, at para. 11.

[119] The parties agree that the relevant date with respect to claim construction is the patent publication date of February 12, 1998.

Further, the parties agree that the Claims of the 630 Patent can be divided into two types: Swiss-type claims and pharmaceutical composition claims.

[120] There are three major areas of dispute: the construction of “infliximab”, the construction of “adjunctive therapy” with MTX, and the construction of “despite already receiving MTX”.

(a) *Infliximab*

[121] As noted by Hospira, “cA2” and “infliximab” are used interchangeably in the 630 Patent. Hospira contended that the 630 Patent is limited to the same molecule as cA2.

[122] However, Hospira fails to consider that this is not the end of the consideration – cA2 is further defined as follows:

> Chimeric A2 anti-TNF consists of the antigen binding variable region of the high-affinity neutralizing mouse anti-human TNF IgGl antibody, designated A2, and the constant regions of a human IgGl, kappa immunoglobulin. The human IgGl Fe region improves allogeneic antibody effector function, increases the circulating serum half-life and decreases the immunogenicity of the antibody. The avidity and epitope specificity of the chimeric A2 is derived from the variable region of the murine A2. Chimeric A2 neutralizes the cytotoxic effect of both natural and recombinant human TNF in a dose dependent manner. From binding assays of cA2 and recombinant human 'l'NF, the affinity constant of cA2 was calculated to be 1 $8x10^{9}M^{-1}$.
>
> (630 Patent at 18.)

[123] Hospira pins its differentiation between cA2 (Remicade) and CT-P13 (Inflectra) on glycosylation differences and the presence of an additional amino acid in CT-P13.

Hospira argued that in 1998 a POSITA would not have considered CT-P13 (Infectra) to be the same molecule as cA2/infliximab (Remicade) and would not have understood differences in glycosylation to be inconsequential.

[124] However, in my view, the expert evidence establishes that the POSITA would not have considered these differences to be relevant to the proper construction of “infliximab”. Even Hospira’s expert on glycosylation, Di Battista, agreed on cross-examination that the 630 Patent did not refer to glycosylation and only defined infliximab in terms of binding to an epitope on human TNF and inhibiting the binding of TNF-α to TNF-α cell surface receptors.

[125] In my view, Di Battista's construction of "infliximab" in the 630 Patent does not exhibit a mind willing to understand, a purposive approach, or a "judicial anxiety" to support a useful invention. He ignored crucial passages of the 630 Patent.

[126] Kennedy submitted that the correct construction of "infliximab" is "a chimeric monoclonal antibody defined by its amino acid sequences set out in the numerous publications cited in the 630 Patent". Kennedy cited the following description of infliximab (cA2) from the 630 Patent:

> [T]he antigen binding variable region of the high-affinity neutralizing mouse anti-human TNF IgG1 antibody, designated A2, and the constant regions of a human IgG1, kappa immunoglobulin…The avidity and epitope specificity of the chimeric A2 [infliximab] is derived from the variable region of the murine A2. Chimeric A2 neutralizes the cytotoxic effect of both natural and recombinant human TNF in a dose dependent manner. From binding assays of cA2 and recombinant TNF, the affinity constant was calculated to be $1.8x0^{9}M^{-1}$.

[127] The defining characteristics referred to in paragraph 122 of high affinity, neutralization and binding to a TNF-α cannot be ignored when constructing the meaning of "infliximab" in the 630 Patent. These characteristics are dictated by the constant and variable regions of the antibody and encoded in their amino acid sequences. This was supported by the expert evidence of Gauldie.

[128] Kennedy concluded that the POSITA would understand that infliximab is defined by its amino acid sequence.

[129] Therefore, I would adopt the construction put forward by Kennedy as it is supported by the entire specification of the 630 Patent and Gauldie's evidence.

(b) *Adjunctive Therapy/Despite Already Receiving MTX*

[130] The parties agree that a patient must be an "incomplete responder" to MTX – meaning that they must have been treated with MTX prior to receiving the anti-TNF-α antibody and been an incomplete responder. The parties also agree that MTX and the TNF antagonist must be present and working at the same time (i.e., adjunctive/concomitant therapy), although there is some disagreement as to what this entails.

[131] The 630 Patent clearly indicates that "TNF antagonists can be administered prior to, simultaneously with (in the same or different compositions) or sequentially with the administration of methotrexate. For example, TNF antagonists can be administered as adjunctive and/or concomitant therapy to methotrexate therapy".

[132] In my view, the proper construction of adjunctive therapy simply requires that the two treatments be present in the patient simultaneously, regardless of sequence or timing of administration.

[133] Hospira's view is that a patient must be receiving MTX alone prior to being treated with the anti-TNF-α antibody in order to be covered by the Claims of the 630 Patent. However, there is nothing in the 630 Patent that indicates that a patient must be treated with MTX alone. In fact, the 630 Patent states that "[o]ther therapeutic regimens and agents can be used in combination

with the therapeutic co-administration of TNF antagonists and methotrexate or other drugs that suppress the immune system". This is clearly inconsistent with Hospira's proposed construction.

[134] Kennedy helpfully provided a chart of "Undisputed Claim Terms" which I adopt for claim construction purposes. This is attached as Appendix A to these Reasons.

[135] For the same purpose, I also adopt Kennedy's Claims Charts and attach it as Appendix B.

C. *VALIDITY OF THE 630 PATENT*

(1) Issue 6: Is the 630 Patent invalid because it is an unpatentable method of medical treatment?

[136] Hospira argued that the 630 Patent claims a method of medical treatment as it is directed towards the "how and when" of using infliximab for the treatment of RA. Infliximab/cA2 was previously known and patented for use in RA, but these patents expired in 2012.

[137] Hospira contended that the Claims of the 630 Patent improperly encroach upon the skill and judgment of medical professionals. Hospira cited *Janssen Inc v Mylan Pharmaceuticals ULC*, 2010 FC 1123, 376 FTR 311 [*Janssen v Mylan*], wherein Barnes J stated as follows:

> [26] What I take from the above authorities is that a patent claim over a method of medical treatment that, by its nature, covers an area for which a physician's skill or judgment is expected to be exercised is not patentable in Canada. This would include the administration of a drug whereby the physician, while relying upon the dosage advice of the patentee, would still be expected to be alert and responsive to a patient's profile and to the patient's reaction to the compound.
>
> …

> [52] In conclusion, I have no doubt whatsoever that the '950 Patent relevant claims cover a method of medical treatment. By attempting to monopolize an effective titration regimen for galantamine, the '950 Patent interferes with the ability of physicians to exercise their judgment in the administration of generic versions of the drug. This is because, absent a license from Janssen, any physician attempting to administer a generic version of galantamine to treat Alzheimer's disease by the method claimed by the '950 Patent would infringe. Indeed, in theory, any physician who attempted to prescribe Reminyl to a patient without Janssen's permission in the manner claimed by the '950 Patent would also infringe.

[138] It is said that the true nature of the alleged invention is disclosed in the 630 Patent through the references to "method for/of treating" RA. Further, the 630 Patent indicates that the doses and intervals disclosed should be adjusted as necessary.

[139] Further, Hospira asserted that the "artificial nature" of the independent Claims, Swiss-type claims and pharmaceutical composition claims ought to be disregarded. This is because the true nature of the 630 Patent is not the manufacture of a medicament or a pharmaceutical composition – "[r]ather, the Claims are directed to the use of an anti-TNF-α antibody in performing adjunctive therapy on an individual suffering from RA whose disease is incompletely controlled despite already receiving MTX (i.e. a method of medical treatment)". Further, the dependant Claims are also not directed towards formulations. Although they are drafted as if to encompass formulations of TNF-α and TNF-α binding Fab fragments, purposive construction shows that they are directed towards a method of medical treatment.

[140] An important aspect of Hospira's position is that a rheumatologist would be restricted by the 630 Patent from using cA2/infliximab to treat an incomplete responder to MTX, but not an

incomplete responder to another DMARD. In addition, the Claims restrict a rheumatologist's ability to monitor and vary treatment. The Claims require a rheumatologist to determine the acceptable dose for a given patient.

[141] The jurisprudence with respect to the unpatentability of methods of medical treatment is not entirely consistent. The prohibition against patenting a method of medical treatment originates with *Tennessee Eastman Co et al v Commissioner of Patents*, [1974] SCR 111, 33 DLR (3d) 459, wherein the Supreme Court of Canada determined that a method of surgical bonding of body tissues with an adhesive composition was unpatentable under the previous *Patent Act*.

[142] In *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77, [2002] 4 SCR 153, the Supreme Court emphasized the necessity that a patent claim be economic and related to trade, industry, or commerce. In that case, the Supreme Court found at para 50 that the claims of the patent which included use did not cover a method of medical treatment because it did not encroach on the skill and judgment of medical professionals:

> The AZT patent does not seek to "fence in" an area of medical treatment. It seeks the exclusive right to provide AZT as a commercial offering. How and when, if at all, AZT is employed is left to the professional skill and judgment of the medical profession.

[143] Swiss-type claims have been upheld by the Federal Court in cases such as *Merck & Co Inc v Apotex Inc*, 2005 FC 755, 274 FTR 113, *Merck & Co, Inc v Pharmascience Inc*, 2010 FC 510, 368 FTR 1, and *AbbVie Biotechnology Ltd v Canada (Attorney General)*, 2014 FC 1251, 471 FTR 164 [*AbbVie*]. In *AbbVie*, Kane J stated as follows:

> [114] The review of the relevant case law supports the appellants' understanding of the principles from the jurisprudence and demonstrates that **the Courts have consistently found that a claim directed to the exercise of professional skill or judgment is not patentable. However, a claim which does not restrict, or interfere with, or otherwise engage professional skill or judgment – including a claim for a fixed dosage and or a fixed dosage schedule or interval- is not impermissible subject matter where there is no evidence to contradict that claimed dosage.** Contrary to the Commissioner's decision and the respondent's position, *Janssen* has not changed the law.
>
> [115] The present claim is for a vendible product. It does not restrict the physician's choice or skill that would be relied on at the outset to determine whether that vendible product should or should not be prescribed. **The case law has established that a use claim may be a vendible product.**
>
> [Emphasis added.]

[144] However, the Federal Court has also held that Swiss-type claims may be unpatentable as methods of medical treatment, such as in *Novartis Pharmaceuticals Canada Inc v Cobalt Pharmaceuticals Company*, 2013 FC 985, 440 FTR 1 [*Novartis*], aff'd 2014 FCA 17, relied upon by Hospira. In *Novartis* at para 101, Hughes J stated that "this Court should disregard the artificial nature of a Swiss claim and look at what is the real subject matter of the claim".

[145] The Court notes that in *Cobalt Pharmaceuticals Company v Bayer Inc*, 2015 FCA 116, 131 CPR (4th) 99 [*Cobalt*], a case wherein the patent did not include Swiss-type claims, Stratas JA questioned whether the policy rationale of the prohibition against patenting methods of medical treatment remains sound:

> [101] The current law in this Court is that methods of medical treatment are not patentable: *Novartis Pharmaceuticals Canada Inc v. Cobalt Pharmaceuticals Company*, 2013 FC 985, 440 F.T.R. 1 at paragraphs 70-101, endorsed by this Court at 2014 FCA 17, 459 N.R. 17, in very brief reasons based on the particular

> arguments made. The provenance of this is *Tennessee Eastman Co. et al. v. Commissioner of Patents*, [1974] S.C.R. 111, 33 D.L.R. (3d) 459, a decision based on former subsection 41(1) of the *Patent Act*, now repealed. In his blog, "Sufficient Description," Professor Norman Siebrasse has forcefully advanced arguments of policy and logic against the current position. In my view, this calls for full consideration by this Court or the Supreme Court in a case where the issue is squarely raised on the facts.

[146] In my view, although the jurisprudence is not entirely consistent, it does establish that Swiss-type claims for vendible products may be patented. The crucial question is whether the Claims of the 630 Patent encroach on the skill and judgment of medical professionals.

[147] I find that the 630 Patent does not cover a method of medical treatment. Taken to its logical end, Hospira's position would prevent an inventor from patenting any subsequent use for a known compound, as this would monopolize the "how and when" of using the compound for treatment – a proposition that is clearly at odds with the system and jurisprudence which allows such new use patents.

Further, the combination of anti-TNF-α and MTX has outcomes that anti-TNF-α alone does not have (i.e., duration of response).

[148] Hospira has not put forward any evidence that a combination is inherently a method of medical treatment or that such a combination is inherently uninventive. Hypothetically, if a new compound X was discovered and patented in 1990, and it was discovered in 2017 that X had an entirely different effect when administered in combination with Y, there is no clear policy rationale that would prevent the discoverer of that combination from gaining the benefit of patent protection simply because the patent protection of the elements of X and Y had expired.

[149] At first blush, Barnes J's comments in *Janssen v Mylan* would appear to favour Hospira's position. In *Janssen v Mylan* at para 4, the claimed "new use" of the cholinesterase inhibitor galantamine was "Janssen's claimed discovery that the slow titration of galantamine improved patient tolerability for the drug, by reducing side-effects and resulted in the ability to use a lower maintenance dose than had previously been shown to be effective".

[150] In my view, there is a distinction to be drawn between the invention in *Janssen v Mylan* (a dosage regime leading to increased efficacy) and the invention in the instant case (a combination of elements leading to increased efficacy and duration of response).

[151] A combination of known elements may properly be the subject of a patent. For example, *Mitchell v Hancock Inspirator Co*, 2 Ex CR 539, 1886 CarswellNat 6 (WL Can) at para 4 (Ex Ct), provides the following aged but on-point statement:

> A new combination of known elements is an invention to all intents and purposes, and as such is patentable and confers on the person having devised such new combination the rights and privileges of an inventor, even if the novelty consisted in a trifling mechanical change, provided, in the latter case, some economical or other result is produced someway different from what was obtained before. The combination then is the invention, and, when patented, is the essence of the patent; it must be taken as a whole, not the elements as several things to be separately discussed, and the combination another thing, but the elements as combined, one thing, to stand with all the privileges conceded by law, and, reciprocally, with all the obligations imposed on all patentees.

[152] Hospira has not provided any rationale supporting its position that the Court ought to "look behind" the Swiss-type claims in this case, beyond the bald assertion that the Claims are "not directed toward the manufacture of a medicament".

[153] This is contrary to the clear words of the 630 Patent, and some further reason should be provided before the Court will ignore the plain wording of the Claims in favour of an alternative explanation.

[154] With respect to the objectives of a rheumatologist being the same as the objectives of the Claims of the 630 Patent, I would reject this argument as contrary to the jurisprudence as described by Hughes J in *Novartis*: "[w]hat the jurisprudence establishes is that a claim to a vendible product, including a substance intended for the treatment of a medical condition, can be good subject matter for a patent claim" (para 91). Clearly, the treatment of a medical condition can be a goal of both medications and of medical practitioners.

[155] In my view, the 630 Patent discloses a vendible product. The plain language of the 630 Patent is directed toward a medicament/pharmaceutical composition.

(2) Issue 7: does the 630 Patent claim improper priority?

[156] Subsection 28.1(1) of the *Patent Act* states:

28.1 (1) The date of a claim in an application for a patent in Canada (the "pending application") is the filing date of the application, unless	**28.1 (1)** La date de la revendication d'une demande de brevet est la date de dépôt de celle-ci, sauf si :
(a) the pending application is filed by	**a)** la demande est déposée, selon le cas :
(i) a person who has, or whose agent, legal representative or predecessor in title has, previously regularly filed	**(i)** par une personne qui a antérieurement déposé de façon régulière, au Canada ou pour le Canada, ou dont l'agent, le représentant

in or for Canada an application for a patent disclosing the subject-matter defined by the claim, or	légal ou le prédécesseur en droit l'a fait, une demande de brevet divulguant l'objet que définit la revendication,
(ii) a person who is entitled to protection under the terms of any treaty or convention relating to patents to which Canada is a party and who has, or whose agent, legal representative or predecessor in title has, previously regularly filed in or for any other country that by treaty, convention or law affords similar protection to citizens of Canada an application for a patent disclosing the subject-matter defined by the claim;	**(ii)** par une personne qui a antérieurement déposé de façon régulière, dans un autre pays ou pour un autre pays, ou dont l'agent, le représentant légal ou le prédécesseur en droit l'a fait, une demande de brevet divulguant l'objet que définit la revendication, dans le cas où ce pays protège les droits de cette personne par traité ou convention, relatif aux brevets, auquel le Canada est partie, et accorde par traité, convention ou loi une protection similaire aux citoyens du Canada;
(b) the filing date of the pending application is within twelve months after the filing date of the previously regularly filed application; and	**b)** elle est déposée dans les douze mois de la date de dépôt de la demande déposée antérieurement;
(c) the applicant has made a request for priority on the basis of the previously regularly filed application.	**c)** le demandeur a présenté, à l'égard de sa demande, une demande de priorité fondée sur la demande déposée antérieurement.

If priority is claimed to a previously filed application, that previously filed application must be the first or earliest application to that subject matter.

[157] Hospira submitted that the 630 Patent improperly claimed priority to United States Application No. 08/690,775 (filed August 1, 1996) [the 775 Patent] when the first or earliest application for co-administration of an anti-TNF monoclonal antibody and MTX was actually United States Application No. 07/958,248 (filed October 8, 1992). In fact, Kennedy had pursued an appeal before the American Patent Office to permit their United States patent application to claim priority to October 1992 – Kennedy's position was that the October 1992 priority disclosed the combination of MTX and anti-TNF-α. Further, the application for the 775 Patent (the August 1996 priority) was a continuation-in-part of earlier applications.

[158] Hospira argued that the claim date for anticipation and obviousness is the Canadian filing date: August 1, 1997. Kennedy failed to introduce the August 1996 priority into evidence and the October 1992 priority covered the co-administration of MTX and TNF-α antibody. Hospira asked the Court to draw an adverse inference against Kennedy in respect of priority.

[159] However, Hospira has not cited any authority to the effect that a previously filed application that is "out of time" will invalidate a claim to a different previously filed application. This is not stated in the *Patent Act* and should not be read into the legislation. Therefore, even if there was an earlier application disclosing the combination of MTX and anti-TNF-α, there is no authority for the position that this would invalid the claim date. As noted by Kennedy, there is no invalidity attack for "improper claim date".

(3) Issue 8: Novelty

[160] The issue of novelty/anticipation was crucial to Hospira's case. In large measure, Hospira contended that all of the developments, writings, papers, and articles in this field in the mid-1990s were directing a POSITA to the invention. They even attack the public awards received by the inventors from their peer groups as unsubstantial because effectively "everyone knew what to do, some had done it", so the inventors did nothing special.

[161] There is a close connection between Hospira's position on novelty/anticipation and its position on obviousness.

[162] Hospira submitted that the invention disclosed by the 630 Patent was anticipated by a number of prior art documents, particularly as identified by Tugwell:

- the Kennedy reports (1994 Kennedy Report, 1994, ARC Report, 1995 Kennedy Report, 1995 ARC Report);
- the T14 Patient Consent Form;
- Higgins;
- Moreland;
- Bologna;
- Elliott 1995; and
- Feldman.

[163] Further, if Hospira's argument that the 630 Patent can only claim priority to the 1997 filing date is accepted, then it is anticipated by several more documents, as identified by Tugwell:

- Kavanaugh Abstract #1; and
- Kavanaugh Abstract #2.

[164] Strand identified the following anticipatory prior art documents:

- the 1995 Kennedy Report;
- the T14 Patient Consent Form;
- Moreland;
- Elliott 1994b; and
- Higgins.

[165] Hospira's arguments are largely directed towards Claim 1 of the 630 Patent. However, Hospira contended that the remaining independent Claims - Claims 2, 17, 18, and 39-42, exhibit only "immaterial differences" from Claim 1 and are therefore also disclosed and enabled by the prior art documents. Further, the dependent Claims are also anticipated as they are "minor [uninventive] variations on the independent claims". Hospira said that "[n]o new technical feature has been disclosed or claimed" and relies on *Merck & Co Inc v Pharmascience Inc*, 2010 FC 510 at para 176, 368 FTR 1.

[166] Kennedy's overall position is obviously that the invention disclosed in the 630 Patent is novel and not anticipated. Kennedy pointed to Hospira's witness Strand's admission that she did not think that any one of these references (referring to Higgins, Moreland, Elliott 1994, the Kennedy Report 1995, and the T14 Patient Consent Form) can contain everything that is in the 630 Patent.

[167] Kennedy's position is that each publication relied upon by Hospira is general, entirely speculative, and suggesting only avenues for future research without any reason to expect success or any enabling detail.

As will be seen, the Court accepts this position as a fair reflection of the evidence.

[168] It is necessary to discuss some of the prior art in detail but without becoming "lost in the forest".

(a) *The Kennedy Reports*

[169] The 1994 Kennedy and ARC reports reference a trial wherein patients will receive a stable low dose of MTX or placebo with monthly infusions of infliximab or placebo. As the trial was not yet complete and there were no results, these reports did not disclose the special advantage.

[170] The 1995 Kennedy and ARC reports reference a trial underway to determine the safety and efficacy of infliximab in combination with MTX. It does not reference the outcome, which could not have been known by the POSITA.

[171] Hospira said that the Kennedy reports must be read together with the Elliott studies such that the common general knowledge would include knowledge that doses of cA2 were known to be effective and safe, and doses of MTX known to treat RA included 7.5 mg/week to 25 mg/week.

[172] These reports do not disclose the special advantage of the invention, nor would they allow the POSITA to practice the invention.

(b) *T14 Patient Consent Forms*

[173] While Hospira said that the T14 Patient Consent Forms disclose the protocol for the clinical study in Example 1 and disclose all elements of Claim 1, these forms are confidential. Even if the forms had entered the public domain, the documents state that the effect of the combination therapy was completely unknown.

[174] Quite apart from the above, these forms would be the subject of the "experimental use" exception referred to in *Novopharm Limited v Eli Lilly and Company*, 2010 FC 915, aff'd 2011 FCA 220 [*Novopharm v Eli Lilly*]. The evidence is that the forms were not intended to be shared more widely than with the patient, immediate family, and treating physician.

[175] Kennedy refers to the recent canvassing and acceptance of the experimental use exception by Justice Fothergill in *Bayer Inc v Apotex Inc*, 2016 FC 1013, 142 CPR (4th) 1 [*Bayer v Apotex*]:

> [157] Section 28.2 of the Act does not provide for an exception for experimental use. However, as recently noted by Justice Hughes in *Bayer v Apotex* at paragraph 119, the law in Canada has long held that there is no public disclosure for the purposes of anticipation where a prior use is experimental (citing *Gibney v Ford Motor Co of Canada* (1967), 2 ExCR 279 at para 49, 52 CPR 140 (Can Ex CT) [*Gibney*] and *Elias v Grovesend Tinplate Co* (1890), 7 RPC 455 at 466). In *Gibney*, Justice Noel held that an inventor may use any means of testing available to him or her, so long as any experimentation is reasonable and necessary, and done in good faith for the purpose of perfecting the invention or testing its merits (*Gibney* at paras 48, 56).
>
> [158] The experimental use exception was also recently canvassed in *Wenzel Downhole Tools Ltd v National-Oilwell Canada Ltd*, 2011 FC 1323, affirmed in part 2012 FCA 333, in which Justice Snider held that the rental of a tool for use in an

oilfield was not experimental, and there was anticipation because the tool had been made available for inspection. She stated at paragraph 90 of her decision that a "use will only be experimental if it is so in the mind of the user". On appeal, the Federal Court of Appeal affirmed Justice Snider's finding on anticipation, but clarified that the test for anticipation by prior disclosure is objective (*Wenzel* at para 118).

[159] In *Bayer v Apotex* at paragraph 119, Justice Hughes noted that the experimental use exception "applies in particular, where, of necessity, the experiment must be conducted in public". He continued at paragraph 121:

> In the present case clinical studies were necessary to prove that the drug was safe and effective and, thereby, gain government approval for sale. Until this had been demonstrated, no commercial sale of the drug could have been made. Bayer took reasonable steps to ensure the confidentiality of the relevant documents and to ensure that unused tablets were returned. The theoretical possibility that some tablets were retained and analyzed is just that, theoretical. This theoretical possibility does not preclude the fact that the studies were experimental, and of necessity, conducted by the provision of tablets to members of the public. Thus these clinical studies are exempted from public use.

[160] Apotex argues that the Phase III trials (including Clinical Trial Nos. 2, 3 and 4) were not experiments conducted to prove that Schering's drug was safe and effective, but were undertaken solely for the purpose of obtaining government approval for commercial sale. According to Apotex, the trials were not necessary for Schering to establish that drospirenone/ethinylestradiol tablets were useful as an effective oral contraceptive, as this had already been established during the Phase II trials. Apotex submits that experiments conducted after an invention has been achieved are anticipatory, and no exception should apply to clinical trials conducted to confirm that the invention works as intended (citing *Gibney* at paras 44, 50).

[161] Bayer responds that its Phase III clinical trials were reasonable and necessary to perfect and test the merits of its invention. Unlike prior studies, the Phase III trials were necessary to evaluate pregnancy prevention in real situations where women were not told to use alternative methods of birth control.

> [162] While I agree with Apotex that the Phase III clinical trials, which are relied upon as the basis for public disclosure, were conducted for the purpose of gaining regulatory approval, this does not, in my view, bring them outside the experimental use exception. The purpose of regulatory trials is, in part, to confirm the safety and efficacy of a proposed drug before it is offered for sale to the public. The risks at this advanced stage have been assessed as minimal, but this does not detract from the inherently experimental nature of a regulatory trial. I agree with Justice Hughes' conclusions in this respect.

[176] The sponsor of the trial took all reasonable steps to maintain confidentiality. This included marking documents as confidential: "[t]he investigator study materials, such as the investigator's brochure and study protocol, are confidential documents intended to be kept confidential by the particular investigator".

[177] There is no substantial evidence that the T14 Patient Consent Forms would also enable the POSITA to practice the invention in order to obtain long-term effective treatment.

(c) *Higgins, Moreland, Feldman, Elliott 1995, Elliott 1994b, and Bologna*

[178] Hospira contended that all these publications disclose all the elements of Claim 1 and the written descriptions, if performed, would infringe Claim 1. This is not the case.

[179] While the Higgins InPharma Bulletin mentions the possibility of combining CDP571 (an anti-TNF-α antibody) with MTX, it does not mention the possibility of combining infliximab with MTX. It also does not disclose the "special advantage" of the combination: reduced HACA responses and improved pharmacokinetics enabling long-term treatment of infliximab with good

efficacy and tolerability. Further, it does not disclose the doses or administration schedule of either infliximab or MTX.

[180] The Moreland paper is directed to clinical studies conducted on cM-T412, a CD4 antibody. Moreland writes, in respect of future considerations, that "we now have the opportunity to combine…TNF inhibitors with MTX, or perhaps other DMARD".

The Moreland paper also contains a warning, that "we should proceed with caution" due to the danger of serious adverse events.

[181] This paper exhibits mere speculation about studies that may be done in the future, without any reference to the special advantage of adjunctive therapy disclosed by the 630 Patent or detail as to how to implement the adjunctive therapy. Therefore, this paper is not enabling.

[182] The Bologna article mentions that the combination of TNF-α inhibition and MTX is a potential area for study, but concludes that it was "still not clear if they provide any genuine benefit". The special advantage is missing from this article, as is detail with respect to how to "deploy" the combination.

[183] Elliott 1994 discusses the results of the T07 extension study, wherein seven RA patients were withdrawn from DMARD therapy. HACA responses were observed in three patients, and the paper concludes that "[t]he application of… combination immunotherapy deserves further investigation in man".

[184] MTX is not mentioned in this article, and the POSITA would not view MTX as a traditional immunosuppressive drug. It is arguable that only hindsight allows Hospira to read up Elliott 1994 as anticipatory. There is disagreement between Schiff and Pisetsky, on the one hand, and Strand, on the other, which suggests that there can be no anticipation.

[185] Elliott 1995 is a review article outlining the positive work that had been done with infliximab therapy by the scientists at Kennedy. It speculates as to potential strategies for dealing with HACA responses, if that should become an issue with infliximab – this includes combination therapy with traditional immunosuppressive drugs as well as combination therapy with anti-TNF-α and anti-CD4 agents. The article does not mention MTX, long-term administration, or trial design.

[186] Feldmann 1996 is a review article which reviews the role of cytokines in RA. It does not mention MTX, but it does describe an ongoing trial of repeated infliximab infusions. It does not disclose the special advantage of combination therapy with anti-TNF-α and MTX.

[187] The Kavanaugh Abstracts, which Hospira said disclose the subject matter of Claim 1, are only relevant if Hospira's argument that the 630 Patent cannot claim priority to the 775 Patent as discussed above is successful. It is not and therefore the publication is after the 630 Patent claim date.

[188] These publications must be set against the legal background. The novelty of an invention is concerned with whether an invention is "new". Subsection 28.2(1) of the *Patent Act* indicates

that the subject matter defined by a claim in an application for a patent must not have been disclosed by the applicant more than one year before the filing date in such a manner as to make the subject matter available to the public or by any other person before the claim date in such a manner as to make the subject matter available to the public.

An oft-referenced shorthand is "what infringes later, anticipates if earlier" (see *Lightning Fastener Co v Colonial Fastener Co*, [1933] SCR 377, [1933] 3 DLR 348 at 352: "what amounts to infringement, if posterior, should, as a general rule, amount to anticipation, if anterior").

[189] In order to establish that an invention was anticipated, Hospira must show that a single reference (a) discloses the nature of the invention and (b) enables the POSITA to perform the invention (*Apotex Inc v Sanofi-Synthelabo Canada Inc v*, 2008 SCC 61 at para 28, [2008] 3 SCR 265 [*Sanofi*]).

[190] With respect to disclosure, the anticipatory prior art must disclose subject matter that would, if performed, infringe the patent under review – at this stage, there is no room for experimentation or trial and error (*Sanofi* at paras 24-25).

[191] With respect to enablement, the Supreme Court of Canada set out in *Sanofi* at para 37 a list of non-exhaustive factors to consider:

> 1. Enablement is to be assessed having regard to the prior patent as a whole including the specification and the claims. There is no reason to limit what the skilled person may consider in the prior patent in order to discover how to perform or make the invention of the subsequent patent. The entire prior patent constitutes prior art.
>
> 2. The skilled person may use his or her common general knowledge to supplement information contained in the

> prior patent. Common general knowledge means knowledge generally known by persons skilled in the relevant art at the relevant time.
>
> 3. The prior patent must provide enough information to allow the subsequently claimed invention to be performed without undue burden. When considering whether there is undue burden, the nature of the invention must be taken into account. For example, if the invention takes place in a field of technology in which trials and experiments are generally carried out, the threshold for undue burden will tend to be higher than in circumstances in which less effort is normal. If inventive steps are required, the prior art will not be considered as enabling. However, routine trials are acceptable and would not be considered undue burden. But experiments or trials and errors are not to be prolonged even in fields of technology in which trials and experiments are generally carried out. No time limits on exercises of energy can be laid down; however, prolonged or arduous trial and error would not be considered routine.
>
> 4. Obvious errors or omissions in the prior patent will not prevent enablement if reasonable skill and knowledge in the art could readily correct the error or find what was omitted.

[192] Disclosure by prior publication, which is at issue in this case, was addressed in *Free World Trust*, wherein the Supreme Court at para 26 adopted the classic statement from *Beloit Canada Ltd v Valmet Oy* (1986), 8 CPR (3d) 289 at 297, 64 NR 287 (FCA):

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

[193] Disclosure does not require the anticipatory document to have been accessed by the public, so long as the public had the opportunity to access the information (*Wenzel Downhole*

Tools Ltd v National-Oilwell Canada Ltd, 2012 FCA 333 at para 68, [2014] 2 FCR 459). Allegedly anticipatory documents should be purposively constructed (*Shire Biochem Inc v Canada (Health)*, 2008 FC 538 at para 64, 328 FTR 123).

[194] In my view, Hospira took an improper approach in its anticipation arguments. Hospira sought to assemble an "anticipatory mosaic" by arguing that one piece of prior art should be read in conjunction with a second piece of prior art that is cited in the first. This is an incorrect approach that ignores the emphasis on a single reference. This approach also conflates anticipation and obviousness. If taken to its logical conclusion, Hospira's approach could lead to anticipation being found in a bibliography.

[195] Further, it would be absolutely remarkable if all of the allegedly anticipatory documents actually anticipated the invention disclosed in the 630 Patent. The evidence does not support that conclusion.

[196] In my view, none of the allegedly anticipatory documents anticipate the invention disclosed by the 630 Patent:

a) Kennedy Reports: Hospira's argument requires that the Kennedy reports and the Elliott studies be "read together" in order for the Kennedy reports to be anticipatory. As discussed above, it is improper to consider two prior art sources together when determining if one piece of prior art anticipates the invention.

Further, it is impermissibly speculative to conclude that because the benefits of infliximab and MTX alone were part of the common general knowledge, that the

POSITA would expect such benefit in combination treatment. That is precisely what is being disclosed by the 630 Patent - to conclude that this was known would be to make a premature finding on obviousness.

b) Higgins: This bulletin simply makes a speculative reference to the possibility of combining MTX and CDP571. It does not disclose the possibility of combining infliximab with MTX and therefore fails at the first stage of the *Sanofi* analysis. It does not disclose the advantage of the combination or a multitude of other elements of the 630 Patent.

c) Moreland: This article references the possibility of combining TNF inhibitors with MTX or another DMARD. In my view, speculation as to future avenues for research is not sufficient to anticipate an invention.

It does not pass the enablement stage of the anticipation analysis because it would not allow the POSITA to perform the invention without "undue burden". The POSITA would be required to design and run clinical trials in order to establish the efficacy of the combination.

In my view, these are not "routine" trials as discussed in *Sanofi*, but would likely be prolonged and arduous as were the actual trials. As discussed above, the POSITA does not have experience drafting trial protocols.

d) Bologna: This article speculates on the possibility of combining TNF-α inhibition and MTX. It does not pass the enablement stage of the anticipation analysis because it would not allow the POSITA to perform the invention without "undue burden".

Similarly, the POSITA would be required to design and run clinical trials in order to establish the efficacy of the combination.

In my view, as with the Moreland article comments, these are not "routine" trials as discussed in *Sanofi*, but would likely be prolonged and arduous. As discussed above, the POSITA likely does not have experience drafting trial protocols.

e) Elliott 1994b: This article discloses the results of the T07 extension study, but it does not disclose the combination with MTX.

f) Elliott 1995: This article discloses the positive work done with infliximab, but it does not disclose the combination with MTX.

g) Feldmann 1996: This article does not disclose the combination with MTX or its special advantage.

h) The Kavanaugh Abstracts: For the reasons provided above, these abstracts are not to be considered because they were published after the claim date.

i) T14 Patient Consent Forms: By claiming that forms may be anticipatory, Hospira either seeks an end to informed consent or to the patenting of medication. It would be contrary to public policy to allow for such a result.

In my view, the circumstances are such that the reasonable person would conclude that the information in the forms was given in confidence (*Novopharm v Eli Lilly* at para 86). The experts were almost unanimous in their evidence that the forms were to be confidential as between the sponsor of the drug, the trial investigators, and the clinical trial patients, their families, and their treating physicians (i.e., Schaible, Strand, Schwieterman, Scott). There was clearly an expectation of confidence in this case, and the industry practice with clinical trials

is to expect the maintenance of that confidence (*Weatherford Canada Ltd v Corlac Inc*, 2010 FC 602 at paras 298-299, 370 FTR 54, rev'd 2011 FCA 2008).

Further, Fothergill J's decision in *Bayer v Apotex* shows that the experimental use exception is not as defunct as Hospira would have one conclude. In the context of Phase III trials, Fothergill J stated as follows at para 162:

> The purpose of regulatory trials is, in part, to confirm the safety and efficacy of a proposed drug before it is offered for sale to the public. The risks at this advanced stage have been assessed as minimal, but this does not detract from the inherently experimental nature of a regulatory trial.

The same reasoning applies, with even greater force, to the T14 Patient Consent Forms for the Phase II trials in the instant case.

(4) Issue 9: Obviousness

[197] The issue of obviousness was also very hotly contested. Hospira claimed that the 630 Patent was obvious or at least obvious to try. It contended many things but principally that the inventors had an easy time coming up with the invention because "everyone knew" it would work.

Before analysing the evidence on this point, it is worthwhile to return to the first principles of the "obviousness" doctrine.

[198] Section 28.3 of the *Patent Act* prohibits the patenting of obvious inventions:

28.3 The subject-matter defined by a claim in an application for a patent in Canada must be subject-matter	**28.3** L'objet que définit la revendication d'une demande de brevet ne doit pas, à la date de la revendication, être

that would not have been obvious on the claim date to a person skilled in the art or science to which it pertains, having regard to	évident pour une personne versée dans l'art ou la science dont relève l'objet, eu égard à toute communication :
(a) information disclosed more than one year before the filing date by the applicant, or by a person who obtained knowledge, directly or indirectly, from the applicant in such a manner that the information became available to the public in Canada or elsewhere; and	**a)** qui a été faite, plus d'un an avant la date de dépôt de la demande, par le demandeur ou un tiers ayant obtenu de lui l'information à cet égard de façon directe ou autrement, de manière telle qu'elle est devenue accessible au public au Canada ou ailleurs;
(b) information disclosed before the claim date by a person not mentioned in paragraph (a) in such a manner that the information became available to the public in Canada or elsewhere.	**b)** qui a été faite par toute autre personne avant la date de la revendication de manière telle qu'elle est devenue accessible au public au Canada ou ailleurs.

[199] In *Sanofi* at para 67, the Supreme Court endorsed a four-step obviousness analysis, succinctly summarized by Kennedy as follows:

1. identify the POSITA and the common general knowledge;
2. identify or construe the inventive concept of the claim at issue;
3. identify the differences between the state of the art and the inventive concept; and
4. determine whether, without any knowledge of the alleged invention as claimed, those differences would have been obvious to the POSITA or whether they required any degree of invention.

[200] In the *Sanofi* framework, the "obvious to try" issue arises at the fourth stage. This test may be appropriate in "areas of endeavor where advances are often won by experimentation" (para 68). *Sanofi* provides guidance as to the application of the "obvious to try" test:

> [69] If an "obvious to try" test is warranted, the following factors should be taken into consideration at the fourth step of the obviousness inquiry. As with anticipation, this list is not exhaustive. The factors will apply in accordance with the evidence in each case.
>
> 1. Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?
>
> 2. What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?
>
> 3. Is there a motive provided in the prior art to find the solution the patent addresses?
>
> [70] Another important factor may arise from considering the actual course of conduct which culminated in the making of the invention. It is true that obviousness is largely concerned with how a skilled worker would have acted in the light of the prior art. But this is no reason to exclude evidence of the history of the invention, particularly where the knowledge of those involved in finding the invention is no lower than what would be expected of the skilled person.

[201] Recently, in *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2017 FCA 76, 146 CPR (4^{th}) 216 [*Bristol-Myers*], the Federal Court of Appeal provided this guidance with respect to the obviousness analysis:

> [65] It may be helpful to keep in mind that the obviousness analysis asks whether the distance between two points in the development of the art can be bridged by the Skilled Person using only the common general knowledge available to such a person. If so, it is obvious. The first of those points is the state of the prior art at the relevant date. References in the jurisprudence to "the

> inventive concept", "the solution taught by the patent", "what is claimed" or simply "the invention" are attempts to define the second point.

[202] Tugwell and Scott, Hospira's experts, were blinded. They were asked what the next logical step in the development of a biologic would have been for an ordinary rheumatologist at the relevant time. Kennedy's experts were not blinded.

[203] Hospira argued that the blinded obviousness opinions of Tugwell and Scott (discussed later) should be accepted over much of the contrary evidence. I have concluded that blinding alone is not a guarantee of reliability and it is not a sufficient reason to prefer the evidence of one witness over another (see *Shire Canada Inc v Apotex Inc*, 2016 FC 382 at para 46, 265 ACWS (3d) 456). Further, given the involvement of the experts in this case in the development of RA treatments during the relevant time period, it is at least questionable whether blinding holds any value. It is impossible to believe that these experts were not aware of the development of Remicade prior to this trial.

[204] Tugwell's evidence was that "the ordinary rheumatologist would have understood that MTX IRs were the largest patient population in a rheumatologists' practice and it was common to add on further therapy to MTX therapy and unethical to remove patients from MTX". A longer-term trial of combination therapy with MTX with MTX incomplete responders would have been the next logical step for development of a biologic. Scott's evidence was that, in terms of commercial development, the next logical step "would have been to conduct a clinical study with cA2 in RA patients taking MTX but not obtaining a satisfactory response from MTX, as described in the 1995 ARC Report".

[205] The expert evidence of Schiff, Pisetsky, and Rubin is more supportable than that of Tugwell and Rubin. In addition, the usefulness of "blinding" is questionable in this case, since "the invention of the 630 Patent – a revolution in RA treatment – and the invention story are world-famous among rheumatologists, netting numerous prestigious awards for the inventors".

[206] I turn now to the four-stage obviousness analysis from *Sanofi* cited in paragraph 199:

1. POSITA and common general knowledge;
2. Inventive concept;
3. State of the Art versus Inventive Concept; and
4. Differences obvious to POSITA.

[207] This formulation of the obviousness issue is consistent with the Court of Appeal's latest formulation of the obviousness analysis found in *Ciba Specialty Chemicals Water Treatments Limited v SNF Inc*, 2017 FCA 225.

(a) *POSITA and Common General Knowledge*

[208] The Court's conclusions on the POSITA and the common general knowledge have been described above.

(b) *Inventive Concept*

[209] With respect to this stage of analysis, in *Bristol-Myers* the Federal Court of Appeal clarified that the inventive concept is not distinct from the solution taught by the patent:

[66] Prior to *Plavix 1*, the jurisprudence followed Beloit and treated the second point as "the solution taught by the patent" which was often treated as synonymous with "what is claimed in the patent" or "the invention": *Proctor & Gamble Pharmaceuticals Canada Inc. v. Canada (Minister of Health)*, 2004 FCA 393, [2005] 2 F.C.R. 269 at para. 47, *Pfizer Canada Inc. v. Canada (Health)*, 2007 FCA 209, 366 N.R. 347 at para. 133, *Novopharm Limited v. Janssen-Ortho Inc.*, 2007 FCA 217, 366 N.R. 290 at para. 25. The question is whether the "inventive concept" was intended to redefine the second point as it was understood to be prior to *Plavix 1*. I note that in the passage from *Pozzoli* quoted above, the English Court of Appeal did not consider the "inventive concept" to have changed anything of substance. If the parties could not agree on it, it could be forgotten. It went on to say at paragraph 19 of its reasons: **"In the end what matters is/are the difference(s) between what is claimed and the prior art." This is essentially the state of Canadian law prior to *Plavix 1*.**

[67] Is it the case that changing one of the two points I referred to earlier amounts to changing the definition of obviousness? Given that obviousness is concerned with whether bridging the difference between the prior art and a second point requires inventiveness, changing the second point will affect the difficulty of bridging that difference, therefore making inventiveness more or less likely. If that is so, is it reasonable to conclude that the Supreme Court intended to change the definition of the obviousness analysis when it adopted, without commentary, the *Windsurfing/Pozzoli* framework? Is it likely that the Supreme Court, having taken great care in modifying the test for obviousness, would, without saying so, change the definition of obviousness?

[68] **My inclination is to believe that the Supreme Court does not change substantive law by implication**, particularly when it has shown a cautious approach to change in the same context: see *Apotex Inc. v. Eli Lilly Canada Inc.*, 2016 FCA 267, 142 C.P.R. (4th) 171 at para. 37.

[69] As an aside, it seems to me that the use of "inventive concept" begs the question which the *Windsurfing/Pozzoli* framework seeks to answer. The question in an obviousness inquiry is whether there has been inventiveness or not. Requiring the Court to identify the inventive concept assumes inventiveness. **It is illogical to ask the Court to identify the inventive concept of the claimed invention and then to ask it to determine if the claimed invention is in fact inventive.**

…

> [75] **For the reasons set out above, I find that the "inventive concept" is not materially different from "the solution taught by the patent".** Had the Federal Court applied that definition to the facts, it would have found that the inventive concept in this case is atazanavir bisulfate, a salt of atazanavir which is pharmaceutically acceptable because it has equal or better bioavailability than the atazanavir free base. Atazanavir's limited bioavailability was the source of the motivation to pursue the solution. The fact that claim 2 of the '736 patent claims a pharmaceutical dosage form of Type-I atazanavir bisulfate confirms its acceptability for pharmaceutical purposes.
>
> [Emphasis added; underlining in original.]

[210] In this case, the parties agree that the inventive concept relates to the use of anti-TNF-α and MTX to reduce the signs and symptoms associated with RA in MTX incomplete responders.

[211] The parties disagree on: (1) whether the inventive concept includes the manufacture of a medicament or a pharmaceutical composition, (2) whether the inventive concept includes long-term efficiency, and (3) whether the inventive concept includes the greater clinical benefit of the combination as opposed to either anti-TNF-α or MTX alone.

[212] In my view, given the decision in *Bristol-Myers* and given the disagreement between the parties, the Court should, at this stage of the analysis, consider "what is claimed in the patent" (i.e., what is the invention). The 630 Patent claims (at Claims 1-2 and dependent Claims, and at Claims 39-40) the manufacture of a medicament using anti-human TNF-α that can be used in combination with MTX in the treatment of RA. It also claims (at Claims 17-18 and dependent Claims) a pharmaceutical composition containing an anti-human TNF-α monoclonal antibody that can be used in combination with MTX in the treatment of RA. That is the inventive concept.

(c) *State of the Art Versus Inventive Concept*

[213] The state of the art is comprised of what could be uncovered by the POSITA conducting a reasonably diligent search (*E Mishan & Sons, Inc v Supertek Canada Inc*, 2015 FCA 163 at paras 20-22, 134 CPR (4^{th}) 207).

[214] In my view, the state of the art is as described by Hospira except with respect to the Higgins InPharma Bulletin and the March 1996 Rheumatoid Arthritis Workshop Proceedings. The Higgins bulletin was written for pharmaceutical industry workers and would not be reviewed by our POSITA, a rheumatologist. The March 1996 Rheumatoid Arthritis Workshop Proceedings were attended by a small number of the top rheumatologists in the world, far removed from the ordinary skilled worker.

[215] Although the Kennedy reports were not published in peer-reviewed journals and were not available on PubMed, the leading medical literature archive, the evidence does indicate that they were available in at least one library. Tugwell, Schiff, and Strand were not aware of the Kennedy reports at the relevant time, although Scott received the ARC reports as he was a recipient of ARC funding.

[216] Nonetheless, I am not satisfied that research methods have progressed to the point where a "reasonably diligent search" would exclude materials of interest available in hard copies in libraries, and I would consider this part of the state of the art.

[217] I also reject Kennedy's suggestion that the Bologna article does not form part of the state of the art. Although the Bologna article is in French, Kennedy has provided no support for its contention that it was in a journal that was "not read" by the POSITA. The POSITA should not be assumed to be unilingual English or be denied access to translation services, particularly in the case of a Canadian POSITA.

[218] As discussed above with respect to the common general knowledge, the state of the art included the efficacy (to some extent) of infliximab in treating RA. MTX was also a commonly used treatment. However, the combination of infliximab and MTX was not disclosed other than in a speculative manner.

(d) *Differences Obvious to POSITA*

[219] Although it may have been reasonable, based on the state of the art, to carry out the combination trials that led to this invention, it was not obvious to do so. A number of potential biologic targets had been identified, and a number of methods of dealing with HACA responses had also been identified – therefore, it was not clear that anti-TNF-α was an appropriate target. It was also not clear what should be done to deal with the shortened duration of response/HACA responses that had been identified in the prior art.

[220] The experts largely agreed that monotherapy was the "holy grail" in terms of biologic development. Further, a combination with MTX was only one of the potential options identified in the prior art.

[221] There was no indication in the prior art that this combination was to be preferred or that it would work to solve the problems identified.

These differences would not have been obvious to the POSITA.

[222] Tugwell and Scott testified that the administration of MTX and cA2 to MTX incomplete responders was the next logical step. However, despite the seemingly clear path forward, only the named inventors took this step.

[223] If this step was as clear as Hospira asserted it to be, it seems strange that it was not taken. The disease was pernicious, the need for a better treatment clear, and the motivation for a solution was high. The Court was impressed with many of the experts in this field and particularly with their dedication to patients and to finding a better treatment.

Given all these forces, the weight of the evidence is that this invention was not obvious even to such dedicated experts, much less to those rheumatologists treating patients – the POSITA.

[224] The factors described in *Sanofi* at para 69 also do not indicate that the invention was "obvious to try".

[225] In *Bristol-Myers Squibb Canada Co v Teva Canada Limited*, 2016 FC 580, 139 CPR (4th) 197, aff'd 2017 FCA 76, the Federal Court discussed the "obvious to try" test as follows:

> [458] The Federal Court of Appeal has subsequently confirmed that the test for whether something is "obvious to try" is **whether it is *more or less self-evident* to try to obtain the invention, and not whether the POSITA had good reason to pursue**

> **predictable solutions or solutions that provide a fair expectation of success**: *Eli Lilly Canada Inc. v. Mylan Pharmaceuticals ULC*, 2015 FCA 286 at para. 4.
>
> [Emphasis added; italics in original.]

[226] Although the POSITA may have had "good reason" to pursue the combination of anti-TNF-α and MTX, it was not self-evident that this combination would work to solve the problem identified in the prior art (i.e., shortened duration of response).

[227] Despite Tugwell and Strand giving evidence that the result was self-evident, this was not the route that they themselves pursued. Tugwell testified that the design and conduct of Examples 1-3 would be "routine", but his evidence was that the POSITA would have experience designing and conducting clinical trials. As discussed above, his view of the POSITA was significantly overqualified and therefore his promise as to POSITA conduct was not well founded.

[228] Centocor, Feldmann, and the FDA may not have been surprised by the results, and may have pursued this path because they believed that the combination would work, but this does not mean that it was self-evident that the invention would work.

[229] Finally, although there was a great deal of motivation to develop a new treatment for RA, it is clear from the literature that this motivation was being pursued in a number of different ways (i.e., trials of different biologics, the majority of which failed).

[230] Therefore, the Court must conclude that the invention was not obvious to try.

(5) Issue 10: Double Patenting

[231] The issue is whether the invention disclosed by the 630 Patent should have been included in Canadian Patent No. 2,146,647 [the 647 Patent], which expired in 2013. The 647 Patent indicated that other anti-inflammatory drugs (such as MTX) could be administered in conjunction with the anti-CD4 antibody or the anti-TNF antibody.

[232] Hospira argued the 647 Patent could have and should have included the subject matter of the Claims in the 630 Patent. In addition, "[i]f the Claims are construed to cover the administration of anti-TNF-α antibodies to patients receiving MTX along with other DMARDs and/or antibodies, the Claims are not patentably distinct from the claims of the '647 Patent".

[233] The law of obviousness-type double patenting was recently summarized by the Federal Court of Appeal in *Mylan v Eli Lilly*:

> [26] The double-patenting doctrine holds that a claim is invalid if it constitutes patenting of an invention that has already been claimed in a previous patent. It is aimed at the problem of evergreening; extending the monopoly that was granted on the first patent by filing a new patent that does not offer a new invention to the public. As such, the doctrine of double-patenting prevents a patentee from violating the bargain at the heart of the patent system.
>
> [27] In *Whirlpool*, the Supreme Court of Canada recognised two types of double-patenting. The first is "same-invention" double-patenting, which occurs when the claims of the second patent are outright "identical or coterminous" to the first. This is not alleged in this case. The second is "obviousness-type" double-patenting, which occurs when the second patent is not identical to the first, but is nonetheless not "patentably distinct" from the first.
>
> [28] Invalidity on the basis of obviousness-type double-patenting is not the same as invalidity on the basis of obviousness.

> Obviousness is directed at the question of whether an "invention" (in the legal sense) exists at all. Obviousness-type double-patenting has a different policy justification; the prevention of evergreening an existing patent through what would otherwise be a valid patent but is, in effect, an extension of the patent that has already been granted: *Merck & Co., Inc. v. Pharmascience Inc.*, 2010 FC 510, at para. 124, 368 F.T.R. 1. . . .
>
> [29] In an obviousness challenge, any piece of prior art, including a collection of works, can be cited as rendering the impugned patent obvious and therefore not patentable: *Sanofi-Synthelabo* at paras. 67-71. By contrast, in an obviousness-type double-patenting challenge, only the earlier patent can be cited as rendering the impugned patent not patentably distinct; any other prior art is only relevant insofar as it contributes to the common general knowledge of the skilled person.
>
> [30] Finally, in an obviousness challenge, subsection 28.3(a) of the *Patent Act* provides that any information disclosed by the patentee within a year prior to the filing cannot be cited as prior art that renders the patent obvious. This effectively gives the patentee a one-year grace period before filing in which it can make disclosures without worrying that those disclosures will be the basis of an obviousness attack. Double-patenting is not subject to subsection 28.3(a), which is what allows the earlier patent to be cited if it was published within a year of the filing date of the impugned patent.

[234] The 647 Patent concerns use of anti-CD4 antibody in conjunction with an anti-tumour necrosis factor antibody for the manufacture of a therapeutic formulation. Claim 1, as described in Strand's first Expert Report at para 257, covers "[u]se of anti-CD4 antibody and anti-tumour necrosis factor (TNF) antibody for the manufacture of a therapeutic formulation for treating autoimmune or inflammatory diseases in a mammal".

[235] Hospira has not established that an entirely different combination, MTX and anti-TNF-α, ought to have been included in this patent.

[236] Further, the two inventions are "patentably distinct" – not only do the patents disclose different combinations, but the 647 Patent discloses a biologic-biologic combination and the 630 Patent discloses a biologic-DMARD combination.

[237] Hospira's obviousness-type double patenting attack is not sustainable.

(6) Issue 11: Sufficiency

[238] Hospira's position is that if the 630 Patent is not anticipated or obvious and if the Court accepts Kennedy's position that the POSITA could not make cA2, then the 630 Patent is insufficient because the POSITA would not have been able to practice the invention as of February 12, 1998.

[239] Further, if the Court does not accept Hospira's argument that the 630 Patent is invalid by reason of disclosure of a method of medical treatment, then Hospira submitted that the Claims are insufficient because "[t]he disclosure of the '630 Patent does not disclose how to perform adjunctive therapy with anti-TNF-α monoclonal antibodies with methotrexate at a dosage or timing of administration over the scope of the claims so as to achieve the Promised Utility".

[240] The *Patent Act* outlines the disclosure requirements for an invention as follows:

27 (3) The specification of an invention must	**27 (3)** Le mémoire descriptif doit :
(a) correctly and fully describe the invention and its operation or use as contemplated by the	**a)** décrire d'une façon exacte et complète l'invention et son application ou exploitation, telles que les a conçues son

inventor;	inventeur;
(b) set out clearly the various steps in a process, or the method of constructing, making, compounding or using a machine, manufacture or composition of matter, in such full, clear, concise and exact terms as to enable any person skilled in the art or science to which it pertains, or with which it is most closely connected, to make, construct, compound or use it;	**b)** exposer clairement les diverses phases d'un procédé, ou le mode de construction, de confection, de composition ou d'utilisation d'une machine, d'un objet manufacturé ou d'un composé de matières, dans des termes complets, clairs, concis et exacts qui permettent à toute personne versée dans l'art ou la science dont relève l'invention, ou dans l'art ou la science qui s'en rapproche le plus, de confectionner, construire, composer ou utiliser l'invention;
(c) in the case of a machine, explain the principle of the machine and the best mode in which the inventor has contemplated the application of that principle; and	**c)** s'il s'agit d'une machine, en expliquer clairement le principe et la meilleure manière dont son inventeur en a conçu l'application;
(d) in the case of a process, explain the necessary sequence, if any, of the various steps, so as to distinguish the invention from other inventions.	**d)** s'il s'agit d'un procédé, expliquer la suite nécessaire, le cas échéant, des diverses phases du procédé, de façon à distinguer l'invention en cause d'autres inventions.

[241] In *Teva Canada Ltd v Pfizer Canada Inc*, 2012 SCC 60, [2012] 3 SCR 625, the Supreme Court affirmed the analysis of the disclosure requirements set out in *Consolboard Inc v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504, 122 DLR (3d) 203, and *Pioneer Hi-Bred Ltd v Canada (Commissioner of Patents)*, [1989] 1 SCR 1623, 60 DLR (4th) 223 [*Pioneer Hi-Bred*].

[242] In *Pioneer Hi-Bred*, the Supreme Court held at 1638 that "[t]he description must be such as to enable a person skilled in the art or the field of the invention to produce it using only the instructions contained in the disclosure".

[243] The POSITA is armed with the common general knowledge as well as a mind willing to understand. In *Uponor AB v Heatlink Group Inc*, 2016 FC 320 at para 187, 139 CPR (4th) 393, Manson J indicated that the standard for sufficiency was set very low.

[244] Hospira's argument with respect to sufficiency is tied to its view of the "promised utility". Given the recent Supreme Court of Canada decision in *AstraZeneca Canada Inc v Apotex Inc*, 2017 SCC 36, [2017] 1 SCR 943 [*AstraZeneca*] and the rejection of the "promise of the patent", Hospira's argument with respect to sufficiency is based on a shaky foundation.

[245] Hospira has not led any evidence that would tend to establish that the 630 Patent is insufficient. Its own experts acknowledge that there is nothing unique or inventive in the way infliximab and MTX have at all times been commercially available.

The doses of both infliximab and MTX as well as the dosing regimens are disclosed in the Examples.

[246] Therefore, I have concluded that the POSITA working with a "mind willing to understand" would be able to practise the invention as of February 1998, using only those instructions contained in the disclosure.

(7) Issue 12: Overbreadth

[247] Hospira argued as a further alternative that, if the Court does not conclude that the Claims are anticipated, obvious, or a method of medical treatment, then they are invalid for being overbroad. This is for the following reasons:

- The Claims are not limited to the dosing and interval of administration laid out in the 630 Patent. This had to be determined by rheumatologists following the approval of cA2.
- Examples 2 and 3 were "conceived independently from the Applicant and named inventors".
- RA is a chronic disease and Kennedy's experts gave evidence that the invention was for long-term therapy. As the Claims also cover single administration, Claims 1-6, 11, 14, 16, 17-22, 27, 30, and 32-42 are therefore overbroad.
- The Examples only established MTX doses of 7.5 mg/wk and 10 mg/wk. The Claims covering doses other than these, Claims 1-10, 13, 16-26, 29, and 32-42, are overbroad.
- To the extent that the mechanism of action is novel or inventive, the Examples do not establish the mechanism of action.

[248] Kennedy counters that the Claims are not overbroad:

> Each of the elements of the claims are well described in the description and each essential element is reflected in the claims. The invention of the 630 Patent is adjunctive therapy with a TNF antagonist and MTX, not the particular TNF antagonist used, nor in what amount. There is no evidence that anti-TNFα antibodies or Fab fragments will not reduce or eliminate the signs and symptoms

> of RA when administered adjunctively to MTX. Hospira's own experts acknowledge that the mechanism of action (binding to an epitope on human TNFα cell surface receptors) was an inherent property of anti-TNF agents.
>
> (Defendant's Closing Submissions at para 173. [Footnotes omitted.])

The named inventors, Maini and Feldmann, confirmed that the combination of anti-TNF-α and MTX could be used to treat RA with efficacy over the long-term.

[249] It is difficult to assess and accept Hospira's position because it has failed to cite any case law or evidence in support of its conclusions. It also failed to cite any jurisprudence on the meaning of "overbreadth" in the context of patent law. Its submissions seem to have been made in the hope that something would "stick" – the patent law equivalent of the Hail Mary pass.

[250] Nonetheless, it seems that Hospira is not making an overbreadth argument in the sense that the 630 Patent claims something that does not work (as discussed in *Alcon Canada Inc v Cobalt Pharmaceuticals Company*, 2014 FC 149 at paras 226-227, 448 FTR 96).

[251] Rather, Hospira is arguing that the disclosure, including the Examples, does not extend to cover the viability of the Claims. This argument on overbreadth was discussed by the Federal Court of Appeal in *Cobalt*:

> [74] One example of overbreadth is where a patent claims more than it sufficiently discloses. If it does, then the overbroad claims are invalid: *Leithiser v. Pengo Hydra-Pull of Canada Ltd.*, [1974] 2 F.C. 954, 6 N.R. 301 (C.A.); *Farbwerke Hoechst Akiengesellschaft Vormals Meister Lucius & Bruning v. Commissioner of Patents*, [1966] Ex. C.R. 91, 50 C.P.R. 220, aff'd [1966] S.C.R. 604.

[252] The Claims are not overbroad:

- The invention discloses the combination of anti-TNF-α and MTX. Hospira has not provided any explanation as to why this combination should be limited to the particular dosages or intervals tested in the Examples. A patent for a pharmaceutical formulation of a medication, for example, would not be limited to the dosages used to test its safety and efficacy. The same reasoning applies with respect to Hospira's contention that the dosages of MTX are not limited to those in the Examples.
- Even if Examples 2 and 3 were conceived by persons other than the named inventors, Hospira has cited no reason as to why this should lead to a finding of overbreadth.
- With respect to single administration, the disclosure established both short-term and long-term efficacy, but it was the long-term efficacy of the combination that was of critical importance given the chronic nature of RA.
- As noted by Kennedy, the mechanism of action for anti-TNF-α was an "inherent property" of anti-TNF agents.

(8) Issue 13: Utility/Promise of the Patent

[253] Hospira had cast its case on utility on the basis of the law of "promise of the patent". After the trial, the Supreme Court of Canada issued *AstraZeneca*, which overturned the "promise of the patent" doctrine developed at the appeal and trial levels of the Federal Courts.

[254] As a result, the Court reopened the submission stage of this trial and the parties took advantage of the opportunity to make submissions on the effect of the Supreme Court of Canada's decision.

[255] Prior to *AstraZeneca*, Hospira had not pursued this argument with much emphasis or vigour. It has subsequently recast its argument to link "promise of the patent" to the absence of sound prediction and to insufficiency and overbreadth.

[256] Rowe J expressed the proper approach to utility in *AstraZeneca*:

> [54] To determine whether a patent discloses an invention with sufficient utility under s. 2, courts should undertake the following analysis. First, courts must identify the subject-matter of the invention as claimed in the patent. Second, courts must ask whether that subject-matter is useful — is it capable of a practical purpose (i.e. an actual result)?
>
> [55] The Act does not prescribe the degree or quantum of usefulness required, or that every potential use be realized — a scintilla of utility will do. A single use related to the nature of the subject-matter is sufficient, and the utility must be established by either demonstration or sound prediction as of the filing date (*AZT*, at para. 56).

[257] The law has returned to the principle that utility is met if a "scintilla" of utility is demonstrated. All the experts agreed that the 630 Patent possessed a "scintilla of utility that related to its subject matter".

[258] Hospira attempts to import the discarded "promise" doctrine into insufficiency and overbreadth. Certainly *AstraZeneca* does not do so and it would be inconsistent to discard that doctrine only to have it resurface under another principle without clear language to do so.

[259] With respect to utility, the 630 Patent gave a new and useful choice supported by three clinical studies showing that treatment with TNF-α and MTX reduced the signs and symptoms of RA.

[260] There is no support for the argument that the 630 Patent did not meet the utility standard set by the Supreme Court of Canada. That should be sufficient to address Hospira's argument.

[261] Linking utility with alleged absence of sound prediction ignores the studies supporting the 630 Patent. Fatal to Hospira's argument is that the Supreme Court of Canada did not require that esomeprazole be better than omeprazole – the drugs in the *AstraZeneca* case.

[262] In respect of insufficiency in relation to utility, it is the Specifications which are the controlling feature. In this present case, a POSITA could follow the steps in the Disclosure and Examples to put the invention into practice. Hospira's reliance on the trial decision in the *AstraZeneca* litigation is misplaced.

[263] In respect of Hospira's position piggybacking the "promise" with overbreadth, particularly in respect of Claims 39-42, the claimed invention has been shown to reduce the signs and symptoms of RA in the three clinical studies included in the 630 Patent. There is no basis for finding overbreadth.

[264] For these reasons, Hospira's new arguments on utility must be rejected.

(9) Conclusion: Validity

[265] Hospira's request that the 630 Patent be declared invalid will be dismissed to be further described in a formal Judgment.

[266] The Defendant shall have their costs. In order to settle costs, the parties shall be entitled to make submissions in writing on all aspects of a cost award.

[267] Matters of injunctive relief, damages, and/or an accounting for profits may be addressed in writing (and, if necessary, an oral hearing may follow) in the context of settling the formal Order for the liability phase of this action.

D. *INFRINGEMENT - COUNTERCLAIM*

(1) Issue 14: Does Inflectra(/Remsima) infringe the Asserted Claims?

[268] Kennedy submitted at trial that the Asserted Claims, Claims 1-3, 5, 6, 9, 10-12, 15, 17-19, 21, 22, 25, 26, 28, 31, 33, and 39-42, are infringed. Hospira is alleged to have infringed the Asserted Claims by making Inflectra and selling it in Canada for the treatment of RA.

[269] In the following paragraphs, the essential elements of the Asserted Claims as identified by Kennedy are underlined, and Hospira's allegedly infringing actions and the evidence thereof are described below.

[270] "TNF-α inhibiting monoclonal antibody" (all Claims).

Inflectra/Remsima contains infliximab, an anti-TNF-α monoclonal antibody, as the active ingredient.

[271] "For performing adjunctive therapy with methotrexate on a patient with active RA whose disease is incompletely controlled despite already receiving methotrexate/on a patient with active RA despite prior therapy with methotrexate and who is already being treated with methotrexate" (all Claims).

Inflectra is only approved for use in patients with RA. Its product monograph lists, as its first indication, the combination with MTX. The recommended dosing regime in the product monograph also indicates that Inflectra should be used in combination with MTX.

[272] Further, the Canadian Rheumatology Association prescribing guidelines and the available literature support the combination of MTX and infliximab.

[273] PLANETRA, the clinical trial by which Celltrion achieved approval of Inflectra, included combination therapy of MTX and Inflectra in patients who were incomplete responders to MTX.

[274] Patients are only reimbursed for treatment with Inflectra if they have failed to achieve satisfactory results by combination treatment with MTX and other DMARDs.

[275] The evidence of Bensen was that of the 20 patients at his clinic receiving Inflectra, 14 had previously been receiving MTX. Hospira's employee, Bamber, indicated that Inflectra patients would have failed MTX treatment.

[276] Kennedy also relied on IMS data to further support the infringement claim.

[277] The IMS data indicated as follows:

> 43 of the 95 Canadian RA patients taking Inflectra had filled a prescription for MTX within 30 days of having been started on Inflectra; 67 of those 95 patients had filled a prescription for MTX within a year prior to having started Inflectra. Since prescriptions generally provide a three-month supply of MTX, a significant proportion of patients on Inflectra were on MTX and continued on MTX up to the point at which they first received Inflectra.

[278] "To reduce or eliminate the signs and symptoms of RA/inhibition of the progression of structural damage, or improving physical function" (all Claims).

As stated in Inflectra's product monograph, Inflectra is approved for "use in combination with MTX for the reduction in signs and symptoms, inhibition of the progression of structural damage and improvement in physical function in adult patients with moderately to severely active rheumatoid arthritis".

[279] "Wherein the TNFα-inhibiting monoclonal antibody (or Fab fragment) (a) binds to an epitope on human TNFα, and (b) inhibits binding of human TNFα to human TNFα cell surface receptors" (all Claims).

The product monograph for Inflectra indicates that "infliximab neutralizes the biological activity of TNFα by binding with high affinity to the soluble and transmembrane forms of TNFα and inhibits binding of TNFα with its receptors".

[280] "Chimeric" (Claims 3, 19).

Infliximab in Inflectra/Remsima is a chimeric antibody.

[281] "Infliximab" (Claims 5, 15, 21, 31, 33).

Kennedy contended that the POSITA would understand infliximab to be defined by its amino acid sequence.

[282] Hospira described the active ingredient of Inflectra as infliximab in its product monograph and marketing literature and therefore Kennedy submitted that Hospira and Celltrion have told Health Canada, doctors, and patients that the active ingredient of their products is infliximab.

[283] As agreed by the experts and the research, the amino acid sequence of Hospira/Celltrion's infliximab is identical to that claimed in the 630 Patent.

[284] Kennedy asserted that the only difference between Hospira's infliximab and Kennedy's infliximab is that Hospira's infliximab has a single additional amino acid at the C-terminal (the non-binding end of the antibody). This is cleaved instantaneously *in vivo*.

[285] Kennedy submitted that the POSITA would have known, in 1998, that this additional amino acid "could not impact the antibody's ability to bind to TNFα and impede binding to TNFα receptors".

[286] In developing its infliximab, Celltrion had purchased and used a cell line which had originated with the cell line that was used to create the infliximab disclosed by the 630 Patent.

[287] Relying on Di Battista's evidence with respect to glycosylation, Kennedy submitted that there is "no material difference between the amounts and types of glycosylation structures present in Hospira's infliximab and those present on the infliximab described in the 630 Patent". Further, there are detectible glycosylation differences even within samples of Hospira's infliximab because of microheterogeneity.

[288] In comparison with the infliximab described in the 630 Patent, Hospira's infliximab exhibits "identical structure, equivalent efficacy, highly similar pharmacokinetics (movement and residence time in the body) and pharmacodynamics (effect in the body), highly comparable immunogenicity, highly comparable binding affinity to TNFα, the identical mechanism of action, highly comparable cytotoxicity and human tissue cross-reactivity".

[289] "TNF-α inhibiting medicine formulated for infusion/spaced at an interval of weeks" (Claims 6, 9, 12, 15, 22, 25, 28, 31).

Remsima/Inflectra are formulated for infusion administration at weeks 0, 2, 6, and every 8 weeks thereafter. They are formulated for infusion at intervals of weeks.

[290] "TNF-α inhibiting medicine formulated for administration as a dosage form containing from about 0.1 milligram to about 500 milligrams of infliximab" (Claim 33)".

Inflectra is supplied in individually boxed 100 mg vials. The recommended dose is 3 mg/kg.

[291] "Methotrexate-containing medicine formulated for administration at intervals of weeks" (Claims 10, 28).

MTX is formulated and prescribed to be administered weekly, either orally or through subcutaneous injection.

[292] Hospira's basic premise is that Kennedy has not discharged its burden of establishing that Hospira infringed the 630 Patent.

Even if the Court construes the Asserted Claims to include the combination of a TNF-α antibody and MTX, Hospira claimed that it has not infringed the Asserted Claims because there is no evidence that Hospira marketed or sold the combination of MTX and Inflectra. Infringement of a combination requires "a taking of the entire combination, i.e. a taking of all the essential elements of the combination as claimed".

[293] Further, Hospira submitted that there are policy considerations at play in the instant case. A generic will not be prevented from obtaining a NOC under the *Patented Medicines (Notice of Compliance) Regulations,* SOR/93-133, simply because there is likelihood that someone will use it for a patented use (*Janssen Inc v Celltrion Healthcare Co, Ltd*, 2016 FC 651 at para 32, 268

ACWS (3d) 639, citing *AB Hassle v Canada (Minister of National Health & Welfare)*, 2002 FCA 421 at paras 56-57, 234 FTR 218).

Hospira said that this rationale ought to apply in the instant case, as there are numerous ways that Inflectra can be administered (even in combination with MTX) without infringing the Claims of the 630 Patent.

[294] Hospira submitted that as the Swiss-type claims refer to the manufacture of a medicament and Inflectra is not made in Canada and is not sold to Hospira in Canada, the Swiss-type claims are not infringed. Further, the pharmaceutical composition Claims cannot be infringed for the same reason.

[295] In addition, Hospira submitted that there is no evidence that Inflectra was manufactured for the performance of adjunctive therapy with MTX to reduce the signs and symptoms of RA. Inflectra is manufactured for use in treating seven diseases and it is not manufactured only for use in RA patients who are already being treated with MTX.

[296] Hospira asserted that adjunctive therapy with anti-TNF-α and MTX in MTX incomplete responders is an essential element of the Asserted Claims. However, Hospira does not use Inflectra in adjunctive therapy and it does not administer Inflectra to patients.

[297] Finally, Hospira submitted that it will not infringe the dependent Claims as follows:

a) Infliximab: The POSITA would understand that infliximab (cA2) is an essential element of the infliximab Claims, and that Inflectra (containing CT-P13) would not infringe these Claims.

b) Inflectra is Not Formulated for Multiple/Repeated Administrations (Claims 9, 10, 12, 15, 25, 26, 28, and 31): Hospira submitted that it does not infringe these Claims because "Inflectra is supplied in 100 mg 'single-use vials' as a lyophilized powder which is reconstituted. It cannot be stored or used at a later date. It is not formulated for multiple and repeated administrations".

c) Hospira/Celltrion do Not Direct the MTX Doses (Claims 12, 15, 28, and 31): Hospira submitted that its product monograph and marketing activities do not influence the dose of MTX used by a rheumatologist or patient.

d) Hospira/Celltrion do Not Direct Administration at Weeks 0, 2, 6, 10, and 14 (Claims 12 and 28): The product monograph refers to administration of Inflectra at weeks 0, 2, and 6, and every 8 weeks thereafter.

[298] It is well recognized that in respect of infringement, Kennedy has the burden of showing infringement, which is a question of fact (*Monsanto Canada Inc v Schmeiser*, 2004 SCC 34 at paras 29-30, [2004] 1 SCR 902 [*Monsanto*]). In *Monsanto*, the Supreme Court stated:

> 35 The guiding principle is that patent law ought to provide the inventor with "protection for that which he has actually in good faith invented": *Free World Trust*, *supra*, at para. 43. Applied to "use", the question becomes: did the defendant's activity deprive the inventor in whole or in part, directly or indirectly, of full enjoyment of the monopoly conferred by law?
>
> [Underlining in original.]

[299] This guiding principle must be kept in mind during the infringement analysis – as the 630 Patent has been found to be valid, Kennedy is entitled to the full enjoyment of the patent monopoly conferred by the 630 Patent.

[300] Hospira has infringed the 630 Patent as set forth in the following paragraphs. The underlined statements are identical to those listed above in the summary of Kennedy's position. Much of the evidence referred to by the Court is in Exhibit P-11.

[301] TNF-α inhibiting monoclonal antibody (all Claims).

Inflectra/Remsima contains CT-P13, an infliximab biosimilar anti-TNF-α monoclonal antibody, as the active ingredient. This is stated in the product monograph: "INFLECTRA™ (infliximab) is a subsequent entry biologic product that consists of a chimeric immunoglobin G1 (IgG1) monoclonal antibody that binds with high affinity to the human tumour necrosis factor alpha (TNFα)".

[302] For performing adjunctive therapy with methotrexate on a patient with active RA whose disease is incompletely controlled despite already receiving methotrexate/on a patient with active RA despite prior therapy with methotrexate and who is already being treated with methotrexate (all Claims).

The product monograph is persuasive evidence that Inflectra(/Remsima) is to be used for the performance of adjunctive therapy with MTX. It states that Inflectra is indicated for "use in combination with methotrexate for the reduction in signs and symptoms, inhibition of the

progression of structural damage and improvement in physical function in adult patients with moderately to severely active rheumatoid arthritis".

[303] On a balance of probabilities, Inflectra is to be used for treatment of MTX incomplete responders. At this time, it is only necessary for the Court to conclude that Inflectra is used in MTX incomplete responders – the extent to which Inflectra is used in MTX incomplete responders is a question best left to the damages phase of this litigation. However, the reimbursement criteria and the IMS data indicate that at least some of the patients receiving Inflectra are MTX incomplete responders. That is sufficient for this infringement analysis.

[304] The IMS data was the subject of objection because it is hearsay. Having admitted the evidence for reasons given at the time, the Court is prepared to rely on that data.

[305] The IMS data does not fall within the business record exception to hearsay for the reasons described in *Eli Lilly Canada Inc v Teva Canada Limited*, 2017 FC 88 at para 18, 279 ACWS (3d) 763:

> In my view, the Deloitte report does not meet the test for the business records exception. That exception requires that the author of the record have a duty to create it, and did so contemporaneously and based on personal knowledge (*Ares v Venner*, [1970] SCR 608 at p 626; see also *Canada Evidence Act*, RSC 1985, c C-5, s 30). Since the author of the Deloitte report is unknown and the details surrounding the report's preparation were not in evidence, the report cannot meet these criteria.

[306] However, the IMS data is information that is commonly put into evidence in patent cases in the Federal Court. I find that this evidence is necessary and reliable.

[307] With respect to necessity, I observe that Kennedy did not call any witnesses with direct knowledge of combination treatment (such as patients or prescribing rheumatologists). Kennedy's witness Bensen was forced to conclude, in cross-examination, that he had no real knowledge of how many patients at his clinics were receiving combination therapy with MTX and Inflectra.

[308] Nonetheless, I find that this IMS data evidence is necessary. A patient or a medical professional would not be able to give the overview provided by the IMS data with respect to the approximate percentage of patients on combination treatment. Bensen attempted, but was ultimately unable, to provide this type of evidence (i.e., are the majority of patients receiving Inflectra also receiving combination treatment?).

[309] Further, this evidence is reliable because, as discussed in *Bradshaw*, it is corroborated by the other evidence in this case. Hospira states that about 100 patients have received Inflectra in Canada. The IMS data is therefore consistent with the party's own admission – it shows that 93 patients have received Inflectra in Canada.

[310] Moreover, the entirety of the evidence put forward in this case tends to confirm the reliability of the IMS data. As noted during the trial, IMS data is a common source of evidence in these types of trials and its reliability is generally accepted by the Federal Court.

[311] <u>To reduce or eliminate the signs and symptoms of RA/inhibition of the progression of structural damage, or improving physical function (all Claims)</u>.

As noted above, the product monograph states that Inflectra is designed for "inhibition of the progression of structural damage and improvement in physical function in adult patients with moderately to severely active rheumatoid arthritis". It is uncontroversial that Inflectra is designed to reduce or eliminate the signs and symptoms of RA.

[312] Wherein the TNFα -inhibiting monoclonal antibody (or Fab fragment) (a) binds to an epitope on human TNFα, and (b) inhibits binding of human TNFα to human TNFα cell surface receptors (all Claims).

Again, the product monograph clearly states that "INFLECTRA™ (infliximab) is a subsequent entry biologic product that consists of a chimeric immunoglobin G1 (IgG1) monoclonal antibody that binds with high affinity to the human tumour necrosis factor alpha (TNFα)".

[313] Chimeric (Claims 3, 19).

It does not appear to be in dispute that Inflectra's infliximab/CT-P13 is a chimeric antibody and this is confirmed in the product monograph.

[314] Infliximab (Claims 5, 15, 21, 31, 33).

As discussed above with respect to claim construction, the POSITA would understand infliximab to be defined by its characteristics and its amino acid sequence. The experts agreed that the amino acid sequence is identical as between the infliximab in Remicade and the infliximab in Inflectra, and that the only difference is a single additional amino acid at the C-terminal in Inflectra's infliximab.

However, for the reasons discussed above with respect to claim construction, I find that this was known by the POSITA to have no impact on function at the relevant time.

[315] TNFα inhibiting medicine formulated for infusion/spaced at an interval of weeks (Claims 6, 9, 12, 15, 22, 25, 28, 31).

Inflectra(/Remsima) is formulated for infusion at intervals of weeks.

[316] TNFα inhibiting medicine formulated for administration as a dosage form containing from about 0.1 milligram to about 500 milligrams of infliximab (Claim 33).

Hospira does not contest that Inflectra is supplied and dosed within this range.

[317] Methotrexate-containing medicine formulated for administration at intervals of weeks (Claims 10, 28).

MTX is formulated and prescribed to be administered weekly.

[318] Although Inflectra may be produced for use in treating diseases other than RA, this does not establish that it is not produced for use in treating RA. I find, on a balance of probabilities, that Inflectra is produced for the treatment of RA in combination with MTX.

[319] As noted above, Hospira had made arguments related to the manufacture and sale of Inflectra/Remsima outside Canada, such that it was not sold to Hospira in Canada, particularly in reference to the Swiss-type claims.

Kennedy urged that this argument be rejected as contrary to the *Saccharin* doctrine, submitting that "infringement occurs if the infringer's activities abroad deprive the patentee to any degree of the full enjoyment of the monopoly in Canada".

[320] With respect to the *Saccharin* doctrine, in *Pfizer Canada Inc v Canada (Health)*, 2007 FC 898, 328 FTR 41, the Federal Court discussed the rationale behind the application of this doctrine:

> [87] I acknowledge that examination of this issue raises the tensions between respect for the territorial limits of patent law and the ability of a country to enforce its own patent legislative scheme in a global market. Companies often use multiple nations to develop, manufacture, market and sell their products. In each of the jurisdictions, there will be a patent scheme that must be respected. However, this should not prevent us, as a matter of Canadian law, from reviewing all aspects of the extra-territorial processes and the products to **determine whether the inventor has been deprived, even in part or even indirectly, of the full enjoyment of the invention.**
>
> [Emphasis added.]

[321] More recently, in *Bayer Inc v Fresenius Kabi Canada Ltd*, 2016 FC 581, 271 ACWS (3d) 829, Brown J stated:

> [24] The Supreme Court of Canada confirmed the application of the *Saccharin Doctrine* in Canadian patent law: *Monsanto Canada Inc v Schmeiser*, 2004 SCC 34 [Monsanto]. The Court said the rule is an "expansive" one, and at para 43 stated that "[i]nfringement through use is thus possible even where the patented invention is part of, or composes, a broader unpatented structure or process". The dissent confirmed at para 155: "[i]t is well established that the use or sale of unpatented subject matter may still infringe a patent where the unpatented subject matter is made employing a patented process: *Saccharin Corp v. Anglo-Continental Chemical Works, Ld.* (1900), 17 R.P.C. 307 (H.C.J.); *F. Hoffmann-Laroche, supra*, at p. 415; *Wellcome Foundation Ltd. v. Apotex Inc.* (1991), 39 C.P.R. (3d) 289 (F.C.T.D.); *American Cyanamid Co. v. Charles E.*

> *Frosst & Co.* (1965), 29 Fox Pat. C. 153 (Ex. Ct.)" [emphasis in original]. The *Saccharin Doctrine* has been recognized to apply to infringement by importation: for example, *Pfizer-Atorvastatin* at paras 80-88.
>
> [Emphasis in original.]

[322] Therefore, in my view it is clear that Hospira cannot escape liability for infringement merely by housing its production overseas. Its position on that matter is rejected.

[323] Hospira has infringed the 630 Patent.

(2) Issue 15: Did Hospira induce infringement of the 630 Patent?

[324] Kennedy submitted that a drug manufacturer may be implicated in the infringement by others for use of a medicine, including infringement by patients.

In the instant case, the Inflectra product monograph is said to amount to "an instruction to infringe". Every reference to RA treatment in the product monograph instructs adjunctive treatment with MTX, and MTX is referred to as a positive influence on treatment.

In addition, the product label (distributed to consumers) states that "INFLECTRA® should be given in combination with methotrexate". The evidence of Kron was that when Inflectra is detailed to doctors, this must be "on-label".

[325] Hospira has three lines of defence to the inducement allegation:

1. there was no direct infringement by third parties;
2. there was no influence by Hospira, which engages again the matter of use of IMS data; and

3. Hospira did not know that infringement would occur.

[326] There is a three-prong test for inducing infringement as held in *Corlac Inc v Weatherford Canada Inc*, 2011 FCA 228 at para 162, 95 CPR (4th) 101:

> First, the act of infringement must have been completed by the direct infringer. Second, 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. Third, the influence must knowingly be exercised by the inducer, that is, the inducer knows that this influence will result in the completion of the act of infringement[.]

[327] Inducement of infringement by others of a claim for a new use of a medicine was discussed by the Federal Court of Appeal in *Novopharm Ltd v Sanofi-Aventis Canada Inc*, 2007 FCA 167, 59 CPR (4th) 24:

> [11] A generic drug manufacturer may be implicated in the infringement by others of a claim for a new use of a medicine if the generic drug manufacturer induces that infringement. Infringement by inducement may be established, for example, by inferences reasonably drawn from the contents of the product monograph for the generic drug product, or evidence relating to the dosage form of the generic product, or its labelling or marketing. However, an inducement to infringe generally cannot be inferred from a mere reference to the new use in the product monograph, for example, in the course of explaining contraindications or drug interactions, or as part of a list of scientific references.

[328] I cannot accept Kennedy's argument that, on the one hand, the 630 Patent is directed toward a drug company and not a practising rheumatologist so it is not a method of medical treatment, and yet, on the other hand, patients will infringe the 630 Patent by receiving adjunctive treatment with MTX and Inflectra. If not for *AB Hassle v Genpharm Inc*, 2003 FC 1443 at para 127, 243 FTR 6, aff'd 2004 FCA 413 ("[i]nfringement of a use patent, under the

Regulations, is not limited to the act of the generic producer; it includes infringement by patients"), I would be disinclined to find inducement.

(a) *Direct Infringement by Third Parties*

[329] In my view, direct infringement by third parties has been established on a balance of probabilities by the same evidence discussed in Issue 14, above. As discussed above, this evidence includes the IMS data.

[330] Hospira argued that a number of conclusions Kennedy wishes to draw from the IMS data are speculative. This may be true if the IMS data were considered in isolation; however, the other evidence in this case (including the product monograph and the product label) supports the interpretation that this data shows that at least some patients are receiving adjunctive therapy with Inflectra and MTX.

[331] Therefore, Kennedy has established, on a balance of probabilities, that patients were taking adjunctive therapy, and the product monograph is strong evidence in favour of the conclusion that Hospira was influencing this outcome.

(b) *Influence by Hospira*

[332] In *Glaston Services Ltd Oy v Horizon Glass & Mirror Ltd*, 2010 FC 1191, 378 FTR 228, Mandamin J stated as follows:

> [89] Inducement has been found in cases where an article is sold to a customer for an infringing purpose, together with instructions

> to use the article in an infringing way. Inducement has also been found where a seller provides a purchaser with instructions or directions for using an infringing method: *Windsurfing International Inc. v. Triatlantic Corporation* (now Bic Sports Inc.), [1984] 63 N.R. 218, 8 C.P.R. (3d) 241 at 264 to 266 (F.C.A.), *Baker Petrolite Corp. et al. v. Canwell Enviro-Industries Ltd. et al.* 2001 FCT 889, [2002] 2 F.C. 3 at paras. 135 to 139 (F.C.T.D.), rev'd on other grounds 2002 FCA 148, [2002] 17 C.P.R. (4th) 478.

[333] In this case, I conclude that the product monograph amounts to instructions or directions for infringement. As discussed in more detail above, it clearly indicates that Inflectra should be used for combination therapy with MTX for the treatment of RA. The product monograph is not speculative – it does not merely list combination treatment with MTX as one option for RA patients, but rather indicates that this is the only option for treating RA. Kron's evidence was that doctors were instructed on-label, meaning that they would not instruct a non-infringing (i.e., monotherapy) method of administering Inflectra for RA treatment.

(c) *Hospira's Knowledge of Infringement*

[334] The product monograph and the evidence of Kron is sufficient to establish, on a balance of probabilities, that Hospira knew that infringement will occur. It is not possible or acceptable that Hospira "turn a blind eye" to what it set in motion.

[335] Further, if it did not know – it ought to have known. In both cases, Hospira is liable.

(3) Conclusion: Infringement

[336] For all these Reasons, Kennedy's claim against Hospira for infringement will be granted.

[337] As discussed under the Validity section conclusions, the parties may make submissions as to costs as well as injunctive and other relief.

[338] The matter of damages or an accounting is to be left to the second part of this case. Kennedy will have the right to elect damages or an accounting of profits.

"Michael L. Phelan"
Judge

Ottawa, Ontario
March 7, 2018

APPENDIX A

Undisputed Claim Terms

anti-human TNFα monoclonal antibody: A monoclonal antibody that binds to human TNFα. The 630 Patent defines "anti-tumor necrosis factor antibody" as one that "decreases, blocks, inhibits, abrogates or interferes with TNC activity *in vitro*." The prefix "anti-" denotes the name of the target the antibody binds to.

anti-human TNFα antibody: An antibody that binds to human TNFα. Where this term is found in the claims, it refers to the prior term "anti-human TNFα monoclonal antibody" and would be understood as synonymous.

anti-TNFα antibody: An antibody that binds TNFα. This term appears in claim 3 and refers to the prior term "anti-human TNFα monoclonal antibody".

human TNFα binding Fab fragment: Defined by the 630 Patent to mean the portion of the antibody that binds to TNFα. According to the 630 Patent, "[t]hese fragments lack the Fc fragment of an intact antibody, clear more rapidly from the circulation, and can have less non specific tissue binding than an intact antibody".

chimeric antibody: The 630 Patent defines "chimeric antibody" as "immunoglobulin molecules characterized by two or more segments or portions derived from different animal species."

monoclonal: The antibody preparation contains a single homogeneous antibody species (whether chimeric, humanized or recombinant) where all individual antibodies have the same amino acid sequence. The monoclonal antibody preparation could be expanded by several methods using various cell sources, but all antibodies so produced would have the identical amino acid sequence and specific binding characteristics.

medicament: A medicine containing an active agent, in this context, a monoclonal antibody or Fab fragment.

signs: A term common in the art for the effects of a disease that physicians can objectively detect, such as joint swelling.

symptoms: A term common in the art for those effects of a disease that the patient subjectively experiences, such as pain or fatigue.

inhibition of structural damage: Therapy was slowing or stopping the progressive joint damage that is generally seen in the x-rays of patients with RA.

improving physical function: An improvement in the patient's ability to carry out daily tasks such as dressing, grooming, rising in the morning, eating, walking and other routine activity. It is related to a reduction in signs and symptoms, especially pain and swelling of joints.

(a) binds to an epitope on human TNFα, and (b) inhibits binding of human TNFα to human TNFα cell surface receptors: How the antibody or Fab fragment works in basic immunology terms. Human TNFα has many epitopes where an antibody may bind. Therefore the 630 Patent indicates that binding the particular epitope must interfere with or inhibit the TNFα from binding to TNFα cell-surface receptors, of which there are likely many. The 630 Patent gives two example epitopes. Both the antibody and its Fab fragments would bind the same epitope. The binding of TNFα so as to block the interaction of TNFα with human TNFα cell-surface receptors is the mechanism by which the activity of TNFα is inhibited.

APPENDIX B

Claims Charts

Claim	Essential Elements
1	(a) use of TNFα inhibiting monoclonal antibody (or Fab fragment thereof) for making a medicine; (b) for performing adjunctive therapy with MTX; (c) on a patient with active RA whose disease is incompletely controlled despite already receiving MTX; (d) to reduce or eliminate the signs and symptoms of RA; (e) wherein the TNFα-inhibiting monoclonal antibody (or Fab fragment) (a) binds to an epitope on human TNFα , and (b) inhibits binding of human TNFα to human TNFα cell surface receptors.
2	(a) use of TNFα-inhibiting monoclonal antibody (or Fab fragment thereof) for making a medicine; (b) for performing adjunctive therapy with MTX; (c) on a patient with active RA despite prior therapy with MTX and who is already being treated with MTX; (d) to reduce or eliminate the signs and symptoms of RA; and (e) wherein the TNFα-inhibiting monoclonal antibody (or Fab fragment) inhibits binding of human TNFα to human TNFα cell surface receptors.
3	The essential elements of claim 1 or 2, where the antibody is chimeric.
5	The essential elements of claim 1-3, where the antibody is infliximab.
6	The essential elements of claim 1-3, or 5, where the TNFα-inhibiting medicine is formulated for infusion.
9	The essential elements of claim 1-3, 5 or 6, where the medicine is formulated for administration multiple times, spaced at an interval of weeks.
10	The essential elements of claim 1-3, 5, 6 or 9, where: (a) the TNFα-inhibiting medicine is formulated for administration multiple times, spaced at an interval of weeks; and (b) the MTX-containing medicine is formulated for administration at intervals of weeks.
12	The essential elements of claim 1-3, 5, 6, 9 or 10, where: (a) the MTX-containing medicine contains 7.5 mg of MTX and is formulated for administration weekly beginning at week 0; and (b) the TNFα-inhibiting medicine is formulated for administration by

Claim	Essential Elements
	infusion at weeks 0, 2, 6, 10 and 14.
15	The essential elements of claim 1-3, 5, 6, 9 or 10, where: (a) the anti-TNFα antibody is infliximab; (b) the TNFα-inhibiting medicine is formulated for administration as a repeated infusion; and (c) the MTX-containing medicine contains 10 mg of MTX.
17	(a) a medicine consisting of a mixture of a TNFα-inhibiting monoclonal antibody and non-medicinal ingredient(s); (b) for use in performing adjunctive therapy with a medicine containing MTX; (c) on a patient with RA whose active disease is incompletely controlled despite already receiving MTX; (d) to reduce or eliminate the signs and symptoms associated with the RA; (e) wherein the TNFα-inhibiting monoclonal antibody (or Fab fragment) (a) binds to an epitope on human TNFα, and (b) inhibits binding of human TNFα to human TNFα cell surface receptors.
18	(a) a medicine consisting of a mixture of a TNFα-inhibiting monoclonal antibody and non-medicinal ingredient(s); (b) for use in performing adjunctive therapy with a medicine containing MTX; (c) on a patient with RA who still has active disease despite prior therapy with MTX and who is already being treated with MTX; (d) to reduce or eliminate signs and symptoms associated with the RA; (e) wherein the TNFα-inhibiting monoclonal antibody (or Fab fragment) inhibits binding of human TNF to human TNFα cell surface receptors.
19	The essential elements of claim 17, where the antibody is a chimeric antibody.
21	The essential elements of claim 17-19, where the antibody is infliximab.
22	The essential elements of claim 17-19 or 21, where the medicine is formulated for administration via infusion.
25	The essential elements of claim 17-19, 21 or 22, where the medicine is formulated for administration multiple times, spaced at an interval of weeks.
26	The essential elements of claim 17-19, 21, 22 or 25, where: (a) the TNFα-inhibiting medicine is formulated for administration multiple times, spaced at an interval of weeks; and (b) the MTX-containing medicine is formulated for administration at intervals of weeks.

Claim	Essential Elements
28	The essential elements of claim 17-19, 21, 22, 25 or 26, where: (a) the MTX-containing medicine contains 7.5 mg of MTX and is formulated for administration weekly beginning at week 0; and (b) the TNFα-inhibiting medicine is formulated for administration by infusion at weeks 0, 2, 6, 10 and 14.
31	The essential elements of claim 17-19, 21, 22, 25 or 26, where: (a) the antibody is infliximab; (b) the TNFα-inhibiting medicine is formulated for administration as a repeated infusion; and (c) the MTX-containing medicine contains 10 mg of MTX.
33	The essential elements of claim 17-19, 21, 22, 25, 26 or 28, where: (a) the antibody is infliximab; and (b) the medicine is formulated for administration as a dosage form containing from about 0.1 milligram to about 500 milligrams of infliximab.
39	(a) use of TNFα-inhibiting monoclonal antibody for making a medicine; (b) for performing adjunctive therapy with MTX; (c) for the reduction in signs and symptoms, inhibition of the progression of structural damage, or improving physical function; (d) in an adult patient with moderately to severely active RA whose active disease is incompletely controlled despite already receiving MTX; and (e) where the TNFα-inhibiting antibody (a) binds to an epitope on human TNFα, and (b) inhibits binding of human TNFα to human TNFα cell surface receptors.
40	(a) use of TNFα-inhibiting monoclonal antibody for making a medicine; (b) for performing adjunctive therapy with MTX; (c) for the reduction in signs and symptoms, inhibition of the progression of structural damage, or improving physical function; (d) in an adult patient with moderately to severely active RA who still has active disease despite prior therapy with MTX and who is already being treated with MTX; and (e) wherein the TNFα-inhibiting antibody inhibits binding of human TNFα to human TNFα cell surface receptors.
41	(a) a medicine consisting of a mixture of a TNFα inhibiting monoclonal antibody and non-medicinal ingredient(s); (b) for performing adjunctive therapy with MTX; (c) for the reduction in signs and symptoms, inhibition of the progression of structural damage, or improving physical function;

Claim	Essential Elements
	(d) in an adult patient with moderately to severely active RA whose active disease is incompletely controlled despite already receiving MTX; and (e) wherein the antibody (a) binds to an epitope on human TNFα, and (b) inhibits binding of human TNFα to human TNFα cell surface receptors.
42	(a) a medicine consisting of a mixture of a TNFα inhibiting monoclonal antibody and non-medicinal ingredient(s); (b) for performing adjunctive therapy with MTX; (c) for the reduction in signs and symptoms, inhibition of the progression of structural damage, or improving physical function; (d) in an adult patient with moderately to severely active RA who still has active disease despite prior therapy with MTX and who is already being treated with MTX; and (e) wherein the TNFα-inhibiting antibody inhibits binding of human TNFα to human TNFα cell surface receptors.

FEDERAL COURT

SOLICITORS OF RECORD

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