Federal Court  Cour fédérale

Date: 20200515

Dockets: T-1163-18
T-220-19

Citation: 2020 FC 621

Ottawa, Ontario, May 15, 2020

PRESENT: The Honourable Mr. Justice Manson

Docket: T-1163-18

BETWEEN:

BIOGEN CANADA INC.,
BIOGEN INTERNATIONAL GMBH AND
ACORDA THERAPEUTICS, INC.

Plaintiffs

and

TARO PHARMACEUTICALS INC.

Defendant

Docket: T-220-19

AND BETWEEN:

BIOGEN CANADA INC.,
BIOGEN INTERNATIONAL GMBH AND
ACORDA THERAPEUTICS, INC.

Plaintiffs

and

PHARMASCIENCE INC.

Defendant

JUDGMENT AND REASONS

I. Introduction

[1] These proceedings involve two patent infringement actions pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133 [the *Regulations*]. The Plaintiffs [collectively Biogen] allege infringement of Canadian Patent No. 2,562,277 [the 277 Patent]. The Defendants, Taro Pharmaceuticals Inc [Taro] and Pharmascience Inc [Pharmascience], deny infringement and allege the patent is invalid for lack of patentable subject matter, anticipation, and obviousness.

[2] The 277 Patent pertains to various uses of fampridine sustained release [SR] formulations and is listed on the Patent Register under the brand name FAMPYRA®. On May 3, 2018, Taro sent Biogen a Notice of Allegation [NOA] pursuant to subsection 5(3) of the *Regulations*. In response, Biogen commenced the action in Court file T-1163-18 on June 15, 2018. Similarly, Pharmascience sent Biogen a NOA pursuant to subsection 5(3) of the *Regulations* on December 20, 2018, and Biogen started the action in Court file T-220-19 on February 1, 2019.

[3] Issues of validity were heard concurrently for both actions, based on the same allegations of invalidity and evidence, along with infringement with respect to Taro. If necessary, the infringement portion of the Pharmascience action is scheduled to take place later this year. This decision and reasons relate to validity of the 277 Patent, and Taro's alleged infringement of the 277 Patent in Court file T-1163-18.

II. Background

A. *The Parties*

[4] Biogen Canada Inc is an Ontario corporation, and Biogen International GMBH is a Swiss corporation. Biogen Canada is a first person within the meaning of subsections 4(1) and 6(1) of the *Regulations*.

[5] Acorda Therapeutics Inc [Acorda], a Delaware corporation, is a small biotechnology company and the registered owner of the 277 Patent. Acorda is joined to this proceeding pursuant to subsection 6(2) of the *Regulations*.

[6] Acorda licenses the 277 Patent to Biogen International, who in turn authorizes Biogen Canada, a related company, to use and sell the invention claimed in the 277 Patent. Biogen Canada markets and sells FAMPYRA in Canada.

[7] Taro and Pharmascience are generic pharmaceutical companies incorporated under the laws of Ontario. Each of these corporations seeks to come to market with its own fampridine SR product in Canada.

B. *Multiple Sclerosis*

[8] Multiple Sclerosis [MS] is a chronic, progressive and unpredictable disease that affects the central nervous system. Damage to the central nervous system interferes with nerve signal transmission between the brain and spinal cord and the rest of the body.

[9] MS is at least in part a demyelinating disease. The myelin sheath acts as an insulating substance that surrounds nerve fibers, which allows electrical impulses from the brain to reach different parts of the body quickly. In its absence, there is a disruption in the transmission of the electrical signals. The insulation myelin provides is akin to insulation for an electrical wire. If the insulation is defective, current in the nerve fiber loses strength.

[10] Part of the known physiology of the disease is leakage of potassium ions in the nerve fiber. Accordingly, blocking potassium ion leakage was a rational target for treatment. Potassium channel blockers such as fampridine were known to restore conduction of action potentials in demyelinated nerve fibers, and as such fampridine had been tested as a potential symptomatic treatment for some MS patients.

[11] MS generally involves two phases. Phase 1 involves attacks of focal neurological dysfunction such as loss of vision, weakness in a limb, and numbness. Phase 2 is commonly called secondary-progressive MS and is amenable to potassium channel blocker treatments. Patients with secondary-progressive MS typically struggle to walk and need assistance to do so, relying on canes, walkers, or part-time wheelchair use.

[12] Impaired walking or walking disability is one of the most commonly reported MS symptoms. Walking impairment can have detrimental effects on patients, and is one sign of the progression of the disease in terms of the practical effect MS has on a patient's daily life.

[13] The Kurtzke Expanded Disability Status Scale [EDSS] is commonly used to express the level of a MS patient's disability. Patients are given a score on a scale from 0 to 10 as summarized below. Scores five through eight are specifically tied to a patient's ability to walk, illustrating the prevalence of this symptom in MS patients:

EDSS Score	Disability
0	Normal
1	No disability
2	Minimal disability
3	Mild to moderate disability
4	Moderate to significant disability
5	Walking disability affects daily life
6	Assistance required to walk
7	Requires a wheelchair
8	Restricted to bed or wheelchair
9	Loss of independence
10	Death due to MS

[14] FAMPYRA and Taro-Fampridine are both indicated for use in adult MS patients with walking disability, defined by an EDSS score of 3.5-7.

[15] MS symptoms are highly unpredictable and vary greatly in type and severity from person to person, and even in the same person over time. Symptoms may come and go or may persist, and often worsen over time. Given the high level of variability, clinical trials in MS patients are challenging. The nature of the disease makes it very difficult to determine whether a potential treatment is having a clinically meaningful effect, or whether any observed change is simply due to the inherent variability of the disease.

[16] To determine whether a given outcome is actually caused by the tested treatment, clinical trials must be placebo-controlled and adequately powered to measure a meaningful response. Due to the inherent variability in MS symptoms, significant variation in the placebo and treatment groups is often seen, which makes it more difficult to detect whether the intervention provides a clinically relevant benefit.

[17] There is no cure for MS. Many approved treatments are aimed at attempting to curb disease progression and manage symptoms. There is no MS treatment that is effective in all patients, so therapies must be tailored to individual patients. In addition to approved treatments, various alternative treatments have been used in the hopes they will provide some relief from MS. Historically, certain alternative treatments have been purported to be “the next best thing” but ultimately have not passed clinical muster. In light of these repeated “false dawns”, MS researchers are highly skeptical of alternative treatments that are not supported by double-blind, placebo-controlled trials.

C. *The 277 Patent*

[18] The 277 Patent is titled “Methods of Using Sustained Release Aminopyridine Compositions.” The named inventors are Andrew Blight, Lawrence Marinucci, and Ron Cohen. The 277 Patent issued from an application filed in Canada on April 11, 2005, claiming priority from United States Patent Application No. 60/560,894, filed on April 9, 2004. It was laid open on October 27, 2005, and issued on January 27, 2015.

[19] The invention claimed in the 277 Patent relates to using SR compositions of potassium channel blockers, specifically aminopyridines, in the effective treatment of various diseases, including MS. The SR composition provides efficacious and safe plasma levels of aminopyridine for a period of up to 12 hours, allowing for twice daily administration while avoiding excessive peaks and troughs in plasma concentration.

[20] In the “Summary of the Invention” section, the patent states that one embodiment of the invention relates to twice daily use of less than 15 mg of aminopyridine for increasing walking speed or improving lower extremity muscle strength in a subject with MS.

[21] The patent further states that one embodiment of the invention relates to a method of selecting individuals based on responsiveness to a treatment. This “responder” or “*post hoc*” analysis was the subject of much discussion during the trial. While the disclosure refers to a method for selecting individuals, this method is not a part of the invention as claimed in the 277 Patent.

[22] The asserted claims relate to the twice daily (also known as “bid”) use of 10 mg of a fampridine SR composition for improving walking (or increasing walking speed) in a subject with MS in need thereof for a period of at least two weeks. Dependent claims add certain pharmacokinetic limitations. Asserted claims 17 to 19, and 21 are exemplary:

> 17. Use of a sustained release 4-aminopyridine composition for improving walking in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
>
> 18. Use of a sustained release 4-aminopyridine composition in the manufacture of a medicament for improving walking in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
>
> 19. The use of claim 15 or 17, wherein the 4-aminopyridine composition exhibits a C_{avSS} of 15 ng/ml to 35 ng/ml.
>
> […]
>
> 21. The use of claim 15 or 17, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 2 to 5 hours after administration of the 4-aminopyridine composition to the subject.

[23] The claims generally break down into two sets: (1) use of fampridine SR for improving walking (or increasing walking speed) in subjects with MS; and (2) use of fampridine SR in the manufacture of a medicament for improving walking (or increasing walking speed) in subjects with MS.

III. Issues

[24] The parties narrowed the issues leading up to trial. The remaining issues are:

A. Does the Acorda S-1 reference anticipate any of claims 17, 18, 23, 28, 31, 32, 37, or 42 of the 277 Patent?

B. Are any of claims 17-19, 21, 23, 24, 26, 28, 31-33, 35, 37, 38, 40, or 42 [the Asserted Claims] of the 277 Patent invalid for obviousness?

C. Are any of the Asserted Claims of the 277 Patent directed to unpatentable methods of medical treatment?

D. Would the making, constructing, using, or selling of Taro-Fampridine by Taro in accordance with its ANDS infringe any of the Asserted Claims of the 277 Patent?

[25] For the reasons that follow, the Acorda S-1 reference anticipates claims 17, 18, 31, and 32, and all of the Asserted Claims of the 277 Patent are invalid for obviousness. None of the Asserted Claims are directed to unpatentable methods of medical treatment.

IV. Fact Witnesses

[26] As a preliminary note, Biogen submitted affidavit evidence from Ms. Preeti Singh and Mr. H. Samuel Frost, but these witnesses were not put forward or cross-examined at trial and their evidence was of no consequence to the determinative issues. The Court notes that their evidence was in the record.

A. *Ron Cohen, MD*

[27] Dr. Cohen is the President and CEO of Acorda and a named inventor on the 277 Patent. He gave evidence of the invention story that led to the 277 Patent.

[28] Acorda initially studied fampridine as a potential spinal cord injury [SCI] therapy using immediate release formulations. Dr. Cohen became aware that Elan, an Irish pharmaceutical company, had developed a SR formulation of fampridine, and in 1998, Acorda took over development of fampridine SR as a treatment for MS from Elan.

[29] Elan had received negative results in a large phase 2 study using fampridine SR in MS patients. The Elan study involved 161 patients with MS receiving escalating doses of fampridine SR from 12.5 mg bid up to 22.5 mg bid.

(1) MS-F200

[30] MS-F200 was a phase 1 study that looked at the safety and efficacy of 5, 15, and 25 mg doses of fampridine SR on oculomotor function in MS patients with internuclear ophthalmoplegia. Acorda hoped to differentiate itself from the Elan study which had failed to show statistical improvement in EDSS and most of its secondary measures. The MS-F200 results were negative. Acorda was forced to consider other endpoints for future fampridine SR studies.

(2) MS-F201

[31] Next, Acorda performed a small phase 2 clinical trial that focused on safety and tolerability at escalating doses of fampridine SR. This study included various secondary outcome measures. MS-F201 was a "hypothesis-generating study."

[32] Doses started at 10 mg bid and escalated to 40 mg bid at a rate of 5 mg each week. Given the small sample size of 36 subjects, this study was insufficiently powered to allow an evaluation of the efficacy of any individual dose compared with placebo. Rather than evaluate efficacy on a dose-by-dose basis, Acorda examined the efficacy endpoints by comparing the pooled data from the fampridine group (all doses combined) with the placebo group, and directly comparing the last measurement during dose escalation.

[33] With the exception of lower extremity manual muscle testing, each of the pre-established endpoints identified in MS-F201 failed, that is, they did not show any statistically significant difference over baseline as compared to placebo. These endpoints included the Timed 25 Foot Walk, a quantitative mobility test based on the time it takes for a patient to walk 25 feet. The results showed large variability, as would be expected, and supported a large placebo effect. Acorda looked to other means of analyzing the data from the study in the hope of finding some other hypothesis from which it could rationalize further studies of fampridine SR.

[34] Acorda reanalyzed the data from MS-F201 and found that scores from two patients were disproportionately influencing the walking times. Looking at walking speed instead of walking

time showed a nominally significant difference from baseline was observed in the pooled fampridine SR treated group compared to the placebo group. These results were reported in the Goodman and Acorda S-1 references, discussed below. Based on these results, Acorda planned a further phase 2 study, MS-F202, to evaluate walking speed.

(3) Acorda's Attempt to Go Public

[35] Following the MS-F201 study, Acorda decided to go public to raise additional funds. Dr. Cohen and Dr. Andy Blight were involved in preparing the business section of the registration statement to be submitted to the US Securities and Exchange Commission [SEC]. This registration statement, now referred to as the "Acorda S-1" is a key document in this litigation.

[36] The Acorda S-1 discloses results from the MS-F201 trial, and the MS-F202 trial design, discussed further below, but states that data for MS-F202 is not expected to be available until March 2004. The signatures on the Acorda S-1 are dated September 23, 2003.

[37] The SEC submission did not garner the desired investment response, and Acorda withdrew the filing in January 2004.

(4) MS-F202

[38] MS-F202 was a phase 2 trial of fampridine SR in the treatment of MS. It was a multicenter, randomized, double-blind, placebo-controlled, parallel-group study in 206 patients with MS. MS-F202 was initiated in February 2003, and completed in December 2003. The study

was designed and powered to compare the efficacy of the three individual doses tested—10, 15, and 20 mg bid—on pre-defined endpoints, including walking speed. Assessments were conducted at five off-treatment visits and four on-treatment visits during the 12-week stable dose period, as shown in the figure below:

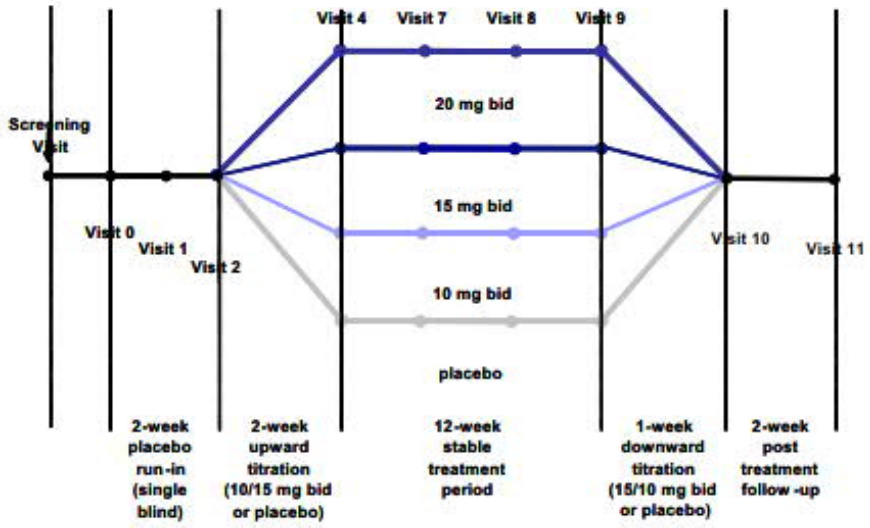

Exhibit 5 to the Affidavit of Dr. Ron Cohen, Figure 1, page 28

[39] MS-F202, as a parallel group study, allowed for statistical comparison between the doses tested. The primary efficacy variable was the percent change in average walking speed during a stable 12-week dose period relative to baseline, using the Timed 25 Foot Walk.

[40] Based on certain pre-defined endpoints, the MS-F202 study failed. There were no statistically significant differences observed in the primary efficacy variable, walking speed, at any of the doses tested. Further, there was no significant difference observed in the protocol specified responder analysis (average change of a magnitude of at least 20%) between any of the fampridine SR doses and placebo.

[41] Unsatisfied with the apparent failure, Dr. Cohen re-evaluated the data. He collected blinded printouts of the walking speed results of all 206 patients for each of the weeks of the study where Timed 25 Foot Walk was assessed and looked at them himself.

[42] Dr. Cohen created a scale, which identified patients as either 0, 1+, 2+, 3+ or 4+, depending on how many on-drug visits were faster than the same patient's fastest off-treatment visit. For this unplanned, *post hoc* analysis, the patients who were faster during 3 of 4 or 4 of 4 on-treatment visits were labelled as "responders," and the others as "non-responders." Dr. Cohen's impromptu *post hoc* analysis looked at *consistency* of response rather than *magnitude* of response. Approximately 36.7% of patients receiving the drug were responders, as compared to approximately 8.5% of patients receiving placebo.

[43] The MS-F202 results showed no meaningful difference in walking speed between the 10 mg, 15 mg and 20 mg bid doses, and showed a slightly increased prevalence of adverse events in the two higher-dose groups. Therefore, Acorda opted to focus on 10 mg bid dosing for phase 3 trials, which took place after the claim date.

V. Expert Witnesses

[44] As a preliminary point, the parties' key witnesses' evidence was uniformly weakened on cross-examination. Given the inconsistencies of evidence, advocacy, and unreasonable positions taken by Drs. Oh and Leist for Biogen, and Drs. Ebers and Bailey for the Defendants, unless otherwise specified, the Court gives limited weight to their expert opinion evidence.

[45] Generally speaking, Drs. Kealey and Williams were credible and helpful witnesses, but their evidence was limited in scope. Dr. Kealey, for the Defendants, gave evidence that the Acorda S-1 document was available to the public as of April 2004. Dr. Williams, for Biogen, opined on whether steady state concentrations of prolonged release drugs can be inferred from single dose bioequivalence studies.

A. *Biogen's Witnesses*

(1) Jiwan Oh, MD, PhD

[46] Dr. Oh is a staff neurologist at St. Michael's Hospital and a scientist at the Keenan Research Center for Biomedical Science in Toronto. Her clinical practice focuses on the treatment of patients with MS, while her research focuses on the use of advanced magnetic resonance imagining techniques in the MS research program at St. Michael's Hospital.

[47] Dr. Oh was qualified to give expert opinion evidence in respect of: neurology; MS; the treatment of MS; drug products used in the treatment of MS (including the pharmacology, formulations and pharmacokinetics of drug products); fampridine; and the design, conduct and analysis (including statistical analysis) of clinical trials (including clinical trials in patients with MS).

[48] Dr. Oh gave evidence on the person of ordinary skill in the art [POSITA], the common general knowledge, and infringement of the 277 Patent by Taro. Dr. Oh took some inconsistent positions between her expert report and cross-examination. For example, on cross-examination

she stated that the product monograph informs her understanding of the claims. She further stated that the *post hoc* responder analysis described in the disclosure is part of the claims. On a plain reading of the claim language, this approach is both incorrect and not credible.

[49] Further, when asked whether anything in the Taro product monograph discusses a type of "responder" analysis, Dr. Oh answered that because the Taro product monograph refers to the FAMPYRA product monograph, the skilled person would import the FAMPYRA product monograph discussion of clinical trials using a *post hoc* responder analysis into the Taro product monograph. Again, this position demonstrates an unreasonable approach in viewing the Taro product monograph in purposive manner.

(2) Roger Williams, MD

[50] Dr. Williams is a consultant in the area of clinical pharmacology, and is board certified in clinical pharmacology and internal medicine. His work experience includes employment at the FDA as the Director in the Office of Generic Drugs from 1990-1993, the Associate Director in Science and Medical Affairs from 1993-1994, the Acting Director in the Office of New Drug Chemistry from 1995-1996, and Deputy Centre Director from 1995-2000.

[51] Biogen submitted Dr. Williams' affidavit in reply to new issues raised by Dr. Bailey. Dr. Williams' only mandate was to respond to paragraphs 17-23 of the Bailey Report, relating to the issue of whether steady state concentrations of prolonged release drugs can be inferred from single dose bioequivalence studies, and indicate points of agreement and disagreement.

[52] Dr. Williams was qualified to give expert opinion evidence in respect of: pharmacokinetics, including steady-state pharmacokinetics of SR products; and bioequivalence and bioequivalence testing, including regulatory standards and approaches in respect thereof.

[53] Dr. Williams was a credible witness.

(3) Thomas Leist, MD, PhD

[54] Dr. Leist is the Chief of the Clinical Neuroimmunology Division and Director of the Comprehensive MS Center at Thomas Jefferson University in Philadelphia, Pennsylvania. He has held these positions since 2000, and has taught neurology as a professor at Thomas Jefferson University since 2014.

[55] Dr. Leist obtained his PhD in Biochemistry from the University of Zurich, Switzerland in 1985, and obtained his MD from the University of Miami in 1993.

[56] Dr. Leist gave evidence on the scientific background of MS, claim construction, the state of the art and POSITA's common general knowledge as of April 2004, anticipation, and obviousness. He also responded to Dr. Ebers' opinions on anticipation and obviousness.

[57] Dr. Leist was qualified to give expert opinion evidence in respect of: neurology; MS; the treatment of MS; drug products used in the treatment of MS (including the pharmacology, formulations and pharmacokinetics of drug products); fampridine; and the design, conduct and

analysis (including statistical analysis) of clinical trials (including clinical trials in patients with MS).

[58] On cross-examination, Dr. Leist stood by the opinions expressed in his report. However, he approached much of the prior art with an apparent mind unwilling to understand. Dr. Leist was evasive in answering simple questions about the prior art cited in his report, particularly with respect to the Goodman Abstracts and Poster. His approach seemed focused on disparaging the cited art that was unfavourable to Biogen to the point that, in his opinion the POSITA would not have learned anything from any of these prior art references.

B. *Defendants' Witnesses*

(1) Burch Kealey, PhD

[59] Dr. Kealey is an associate professor of accounting at the University of Nebraska at Omaha. His opinion evidence relates solely to the date on which Acorda S-1 would have been available to the public through the SEC EDGAR database, and how many times this document was accessed between its release date and April 11, 2004.

[60] Dr. Kealey was qualified to give expert opinion evidence on the public availability of financial documents provided to the SEC EDGAR electronic database and the extent to which such documents were publicly disseminated through EDGAR.

[61] Dr. Kealey was a credible witness.

(2) George Ebers, MD

[62] Dr. Ebers is an Emeritus Professor at the Nuffield Department of Clinical Neurology at the University of Oxford. He gave evidence on the scientific background regarding MS, the POSITA and their common general knowledge, claim construction, the state of the art as of April 2004, anticipation, and obviousness.

[63] Dr. Ebers is trained as a consultant neurologist and medical doctor. He practiced as a neurologist and taught as a Professor at Western University from 1977 to 1999, treating patients with MS and general neurology patients during that period. His research at Western focussed on epidemiology, genetics, natural history and clinical trials in MS. He has been head of the Department of Clinical Neurology at Oxford since 1999, and has continued practicing medicine.

[64] Dr. Ebers estimates that he has seen between six and seven thousand MS patients over the past four decades. He was responsible for the MS Clinic in London, Ontario, which became the largest in the world under his direction, and co-founded and developed the Canadian MS Clinic Network. In these roles, he actively participated in clinical trials and the evolution of knowledge about this disease and its treatments.

[65] Dr. Ebers was qualified to give expert opinion evidence about MS; the etiology of MS; the progression of MS; the treatment of MS and its symptoms; the role of potassium channel blockers in the treatment of MS; the use of drugs, including fampridine, in the treatment of the

symptoms of MS; the design, conduct and analysis of clinical trials related to MS; and the use and pharmacokinetics of SR drug products used to treat MS.

[66] While the parties agreed on his qualifications, Dr. Ebers admitted on cross-examination that he does not consider himself an expert in the role of potassium channel blockers in the treatment of MS, or the pharmacokinetics of SR drug products used to treat MS.

[67] Dr. Ebers' testimony on the history of MS and treatments for MS was believable and detailed. He has clearly dedicated much of his life to studying and documenting MS and treatments for the disease.

[68] However, Dr. Ebers testimony related to the state of the art and obviousness was weakened on cross-examination. When taken to the prior art he cited in his report, he disparaged virtually every study put forward as prior art, labelling them as speculative, poorly designed, and limited by the small number of patients tested.

[69] Given his long history in treating MS and the repeated occurrence of "false dawns," Dr. Ebers was understandably skeptical of purported new treatments. That said, his unbridled skepticism weakened his opinion, as he appeared to see no value in many of the studies put to him, including those cited in his own report, and the studies conducted in the development of the 277 Patent.

[70] Dr. Ebers' report was also far from impartial. Biogen highlighted approximately one hundred paragraphs of his report that were copied nearly verbatim from Taro's NOA, which Dr. Ebers acknowledged he had never reviewed.

[71] It is certainly permissible for counsel to help an expert prepare his or her report (*Moore v Getahun*, 2015 ONCA 55 at paras 55, 64). Counsel may even point the expert to relevant prior art, as long as the expert reviews and confirms the content of his or her report, as the choice of prior art is entirely in the hands of the party alleging obviousness (*Ciba Specialty Chemicals Water Treatments Limited's v SNF Inc*, 2017 FCA 225 at para 60). It is quite another story for an expert to do little or no independent research and accept, verbatim, large portions of a NOA prepared by legal counsel which the expert has never seen, let alone reviewed. This crosses the line of propriety and puts into real doubt the impartiality and independence of the expert; key aspects of the expert's duty to the Court (*White Burgess Langille Inman v Abbott and Haliburton Co*, 2015 SCC 23 at paras 26-32).

(3) David Bailey, PhD

[72] Dr. Bailey is a clinical pharmacologist at the Lawson Health Research Institute and a Professor Emeritus in the Department of Medicine, Clinical Pharmacology at Western University in London, Ontario.

[73] Dr. Bailey's area of research includes pharmacokinetic drug interaction investigations, specifically looking at pharmacokinetic parameters such as those measured in bioequivalence studies.

[74] Dr. Bailey was qualified to give expert opinion evidence on the pharmacokinetics of SR drug products, including steady-state pharmacokinetics of SR products. He responded to Dr. Oh's infringement opinion on whether steady state concentrations of SR drug products can be established from single dose bioequivalence studies.

[75] Dr. Bailey was, in his own words, passionate. However, at times on cross-examination he was obstructionist, answering counsel's questions with further questions. On multiple occasions he avoided answering straightforward questions by talking about his own research and numerous publications.

VI. Claim Construction

[76] Claim construction is a matter of law for the judge, and claim construction is antecedent to consideration of both infringement and validity issues (*Whirlpool Corp v Camco Inc*, 2000 SCC 67 at paras 43, 61 [*Whirlpool*]). The same construction of the claims applies to issues of infringement and validity (*Whirlpool*, above, at para 49).

[77] Where the judge can construe the patent as it would be understood by a skilled person, expert evidence is not required (*Pfizer Canada Inc v Canada (Minister of Health)*, 2007 FC 446 at paras 25, 35-36; *Excalibre Oil Tools Ltd v Advantage Products Inc*, 2016 FC 1279 at para 119).

[78] The principles of claim construction were laid out by the Supreme Court of Canada in *Whirlpool* and *Free World Trust* (*Whirlpool* at paras 49-55; *Free World Trust v Électro Santé*

Inc, 2000 SCC 66 at paras 44-54 [*Free World Trust*]). Claims are to be read in an informed and purposive way, with a mind willing to understand and viewed through the eyes of a POSITA having regard to the common general knowledge. The entire patent specification should be considered in order to ascertain the nature of the invention, however adherence to the claim language allows the claims to be read in the way in which the inventor is presumed to have intended, promoting fairness and predictability.

[79] The relevant date for construing the claims is the publication date: October 27, 2005.

A. *Person of Ordinary Skill in the Art [POSITA]*

[80] The parties generally agreed that the 277 Patent is directed towards a skilled team comprising a clinician with experience treating MS patients, an individual with a basic understanding of pharmacokinetic parameters, a pharmaceutical formulator with experience with SR formulations, and an individual with experience in the design and analysis of clinical trials.

[81] Dr. Ebers opined that the POSITA team would also include support staff who monitor publicly available information, including patent literature, press releases and/or technical documents relating to fampridine and other disease modifying therapies for MS.

[82] Biogen disputes Dr. Ebers' inclusion of this "searcher" or "support staff" member of the POSITA team. I agree. The POSITA is a worker of ordinary skill "in the art to which the patent relates" (*Whirlpool* at para 53).

[83] It is well accepted that the notional POSITA may be a team of persons with different skills (*Pfizer Canada Inc v Pharmascience Inc*, 2013 FC 120 at para 28). However, the notional team must still be made up of workers of ordinary skill in the field to which the patent relates. Regardless of whether a drug development team would practically include support staff whose job it was to search the patent literature and press releases, the patent at issue does not relate to the field of patent searching. The patent relates to the treatment of MS, and the make up of the composite POSITA should reflect as much.

[84] Having considered the expert testimony on the composite POSITA, I find that the 277 Patent is directed to a POSITA team with expertise in the treatment of MS, design and analysis of MS clinical trials, and pharmaceutical formulations. Further, the POSITA understands basic pharmacokinetic parameters and biostatistics. No expert pharmacokineticists or biostatisticians were put forward as witnesses for claim construction, so I accept that the skilled MS clinician/neurologist would have sufficient expertise in these areas to understand and interpret the 277 Patent.

[85] The skilled team does not include support staff who monitor publicly available information such as the patent literature and other technical documents.

B. *Common General Knowledge*

[86] While acknowledging that the relevant date for claim construction is October 27, 2005, Drs. Ebers and Leist both outlined the common general knowledge as of April 2004, the relevant date for assessing anticipation and obviousness. Neither party advanced evidence that the

common general knowledge changed appreciably between April 2004 and October 2005, so for the purpose of claim construction, the common general knowledge will be taken to be the same as of both of these dates.

[87] The common general knowledge includes at least the background on MS discussed at the outset of these reasons, in addition to knowledge of fampridine as it relates to MS treatment, as detailed below.

[88] As part of their common general knowledge, the POSITA would have been aware of fampridine's postulated mechanism of action, and that this drug had potential utility in various central nervous system disorders, including SCI and MS.

[89] The POSITA would known that MS was not a stereotypical disease, with substantial variability both between individuals (inter-individual variability), and within individual patients (intra-individual variability) on a weekly and sometimes daily basis. Due to this variability, a drug substance may provide significant improvement in one individual and have little to no effect in another.

[90] Studies had shown that stable MS patients can experience day-to-day variability in Timed 25 Foot Walk results of up to 20%. Accordingly, some researchers used a threshold of a 20% improvement at a statistically significant level as a minimum requirement when evaluating whether a given intervention caused a particular effect, as opposed to chance improvement due to variability.

[91] The POSITA would have been aware that MS is a debilitating progressive chronic disease. Where symptomatic treatments like fampridine are used, long-term or continuous administration is required to see continued benefit. Fampridine was thought to have a narrow therapeutic window, and higher doses of fampridine were associated with serious adverse effects, including seizures. When selecting a proper dose of fampridine, the POSITA would have been aware of potential adverse effects, and the "start low, go slow" approach to therapy was commonly used. Many clinical studies using fampridine started patients at a low dose before titrating the patient up to higher levels.

C. *Claim Terms Needing Construction*

[92] As stated above, the claims generally break down into two sets: (1) use of fampridine SR for improving walking (or increasing walking speed) in subjects with MS at a unit dose of 10 mg bid; and (2) Swiss-type claims for the use of fampridine SR in the manufacture of a medicament for improving walking (or increasing walking speed) in subjects with MS at a unit dose of 10 mg bid. Dependent claims add further limitations, namely specific pharmacokinetic parameters and administration timing.

[93] All relevant claims of the 277 Patent are reproduced in Appendix A. For ease of reference, independent claim 17 reads:

> Use of a sustained release 4-aminopyridine composition for improving walking in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.

[94] The Asserted Claims use plain, simple terms. The Court generally does not need expert assistance in order to understand the terms "10 mg twice daily," "improving walking," "increasing walking speed," and "subject with MS in need thereof." The POSITA would have understood these terms at the relevant date as follows:

> **Improving walking** includes improving some aspect of walking, such as endurance, step strength, or walking speed. The improvement must be quantitatively measured, and given the variability of symptoms and the prevalence of placebo effect in MS treatment, the quantitative improvement must be statistically significant.
>
> **A subject with MS in need thereof** refers to MS patients who experience some form of walking disability. This is necessarily a subset of all MS patients, as patients with little to no disability (e.g. EDSS scores 0 – 2) are not in need of improvement walking, and patients who are immobilized (e.g. EDSS scores 8 – 9) are no longer able to walk, and will not benefit from treatment to improve walking. Therefore, a subject with MS in need of treatment is a subject with an EDSS score of approximately 3.5 to 7.
>
> **For a time period of at least two weeks** means the fampridine SR is used for at least two weeks, at a fixed dose of 10 mg bid.
>
> **Unit dose of 10 milligrams of the 4-aminopyridine twice daily** means the dose amount is 10 mg twice daily, or 10 mg bid.

[95] The improvement in walking or increase in walking speed need not be "clinically meaningful," as argued by Biogen. Although Dr. Leist opined that the POSITA would only consider walking to be improved if a quantitative improvement also had a perceived benefit to the MS patient, on a purposive construction such a subjective element does not form part of the claimed invention.

[96] In arguing for a construction that includes a clinically meaningful improvement in walking, Biogen invites the Court to include a qualitative indicia that engages the skill and

judgment required to gauge the subjective perceived benefit to a given patient in the context of the physician-patient relationship, thus treading into the territory of an unpatentable method of medical treatment. Moreover, inclusion of a subjective element would make it nearly impossible to establish infringement, as the patentee would need to show that any given patient would perceive a benefit in their walking or walking speed.

[97] Further, I do not accept Biogen's argument that the claim limitation "for a time period of at least two weeks" requires that walking be consistently improved. The plain claim language merely requires use of 10 mg bid fampridine SR over the entire two week period.

[98] Independent claim 18 is a Swiss-type claim that is otherwise identical to claim 17. The experts agreed that claim 18 and its dependent claims cover the activities of a pharmaceutical manufacturer.

[99] Independent claims 31 and 32 mirror claims 17 and 18, but claim use of fampridine SR "for increasing walking speed" rather than "improving walking." The experts agreed that increasing walking speed is narrower than improving walking.

[100] Dependent claims 19, 24, 33, and 38 add the further limitation that the fampridine SR composition exhibits a C_{avSS} of 15 ng/mL to 35 ng/mL. I accept Dr. Ebers' evidence that C_{avSS} means average plasma concentration at steady state.

[101] Dependent claims 21, 26, 35, and 40 add the further limitation that the fampridine SR composition provides a mean T_{max} in a range of 2 to 5 hours after administration. As defined in the disclosure, T_{max} is the "time to maximum plasma concentration."

[102] Dependent claims 23, 28, 37, and 42 state that the fampridine SR composition is in a form for administration every 12 hours, further limiting "twice daily" administration.

[103] Each of the asserted dependent claims also depends from earlier unasserted claims. These unasserted claims are broader in that they do not include the element "for a time period of at least two weeks" (claims 15, 16, 29, and 30), and some of the claims specify a broader mean T_{max} range of 1 to 6 hours or 2 to 6 hours after administration (claims 20, 22, 25, 27, 34, 36, 39, and 41).

[104] As a final note on claim construction, to the extent that Biogen's experts advocated for reading the *post hoc* responder analysis from the disclosure into the claims, this approach is incorrect. Drs. Oh and Leist both proffered such a tortured construction, attempting to read the responder analysis into the Asserted Claims.

[105] As detailed in the Agreed Statement of Facts, the 277 Application included claims to the use of a fampridine SR composition, and claims to a method for selecting individuals based on responsiveness to treatment. In an August 26, 2011 Office Action, the patent examiner objected to the claims as filed for being directed to a plurality of inventions. In its February 27, 2012 response to the Office Action, Acorda elected to proceed with the use claims in the 277

Application, and file a divisional application for the method claims for selecting so-called responders. The divisional application remains in good standing with the Canadian Intellectual Property Office.

[106] Throughout the trial, Biogen characterized the divisional application as "forced." This is an overstatement, as the August 26, 2011 Office Action was an objection, rather than a rejection by way of a "final action." At this point in the prosecution process, Acorda's election to proceed with the use claims and file a divisional for the method claims was voluntary. If Acorda felt that the unity of invention objection was not merited, it could have advocated that the responder method was indeed part of the claimed use invention.

[107] The responder analysis method claims that were divided out into the pending divisional application may have merit, but those claims are clearly not before the Court.

[108] To its credit, Biogen did not advance this construction in its closing argument, acknowledging that the responder analysis is not part of the claims as construed or the inventive concept, but does form part of the inventors' course of conduct.

[109] In summary, the essential elements of claims 17 and 18 are:

i. Use of a fampridine SR composition (or use of a fampridine SR composition in the manufacture of a medicament)
ii. For improving walking in a statistically significant way
iii. In a subject with MS who experiences some form of walking disability

iv. For a time period of at least two weeks

v. At a unit dose of 10 mg bid.

[110] The remaining Asserted Claims incorporate one or more of the following essential elements:

i. Increasing walking speed in a statistically significant way (claims 31 and 32)

ii. The fampridine SR composition exhibits a C_{avSS} of 15 ng/mL to 35 ng/mL (claims 19, 24, 33, and 38)

iii. The fampridine SR composition provides a mean T_{max} in the range of 2-5 hours after administration (claims 21, 26, 35, and 40)

iv. The fampridine SR composition is in a form for administration every 12 hours (claims 23, 28, 37, and 42).

[111] As noted, the asserted dependent claims also depend from earlier unasserted claims that do not include the element “for a time period of at least two weeks,” and/or specify a broader mean T_{max} range of 1 to 6 hours or 2 to 6 hours after administration.

VII. Validity Attacks

[112] The 277 Patent is presumed to be valid (*Patent Act,* RSC 1985, c P-4, s 43(2)). The Defendants bear the burden of establishing each ground of invalidity on a balance of probabilities (*Diversified Products Corp v Tye-Sil Corp,* (1991) 35 CPR (3d) 350 at 357-359 (FCA)).

[113] The cut-off dates for citable prior art are April 11, 2004 for inventor-derived disclosures, and April 9, 2004 for disclosures not derived from the inventors (*Patent Act*, ss 28.2 and 28.3).

A. *Anticipation*

[114] Pursuant to section 2 of the *Patent Act*, an invention must be novel. Patent claims are anticipated if a single prior art reference both discloses and enables the claimed invention (*Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at paras 25-27 [*Sanofi*]).

[115] These two requirements were recently described by the Federal Court of Appeal as follows (*Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2020 FCA 30 at para 66 [*Hospira*]):

> 1) The prior art reference must disclose the claimed invention such that, if performed, it would necessarily result in infringement; and
>
> 2) The prior art reference must be sufficiently detailed to enable a [POSITA] to perform the claimed invention without the exercise of inventive ingenuity or undue experimentation.

[116] At the disclosure stage of the analysis there is no room for trial and error or experimentation by the POSITA; they are simply reading the prior art in order to understand it (*Sanofi*, above, at para 25). The allegedly anticipatory art need not describe the claimed invention exactly (*Abbott Laboratories v Canada (Health)*, 2008 FC 1359 at para 75, aff'd 2009 FCA 94).

(1) Prior Art References

[117] Prior to trial, the parties provided the Court with a joint statement of issues, which states that the Defendants only assert the Acorda S-1 document with respect to anticipation.

[118] At the outset of closing submissions, counsel for Taro rose to explain this was never the Defendants' intention. An earlier draft of the joint statement of issues had additionally listed the Goodman Abstracts and Goodman Poster as relevant references for anticipation, and agreeing to the finalized joint statement of issues without these additional references was an oversight resulting from a miscommunication between counsel.

[119] Having considered the parties' submissions made prior to closing submissions, the Goodman references will not be applied for anticipation. The joint statement of issues explicitly states that only the Acorda S-1 is being asserted for anticipation, and Biogen ran its case on this basis. To open the anticipation art up to additional documents after the evidentiary phase and after written submissions were submitted would be unfair and prejudicial to Biogen.

[120] In any event, the Goodman references disclose much of the same information from the MS-F201 results disclosed in the Acorda S-1, which is in play for determining anticipation.

[121] The Acorda S-1 is a financial document filed by Acorda with the SEC. Based on Dr. Kealey's evidence, the Acorda S-1 was available to the public prior to April 2004. Dr. Kealey's evidence is consistent with Dr. Cohen's testimony that Acorda prepared and filed the S-1

document in an effort to garner public investment, and ultimately withdrew the filing in January 2004 because investor response was lower than Acorda had hoped for.

[122] The Acorda S-1 describes the MS-F201 and MS-F202 studies, stating that MS-F201 was completed in 2001, and MS-F202 was initiated in early 2003, with results anticipated by the end of March 2004. The studies were conducted in cooperation with Elan, with Elan supplying the fampridine SR composition.

[123] As stated in the Acorda S-1, MS-F201 was designed to determine the optimal dose level of fampridine SR and to evaluate possible ways to measure the effect of the drug, including motor strength, timed walking, and self-reported fatigue. Subjects with MS received fampridine SR in doses increasing from 10 mg to 40 mg bid over eight weeks of treatment. The results are described as follows:

> The clinical trial demonstrated that doses up to 25 mg twice a day were well tolerated, and were associated with statistically significant improvements in walking speed and leg muscle strength. Most of the improvement in strength and walking speed was apparent within the first three weeks of the Fampridine-SR treatment, at doses from 10 to 25 mg twice a day.

[124] The Acorda S-1 describes MS-F202 as a clinical trial designed to compare doses of 10, 15, and 20 mg bid, and to assess their relative safety and efficacy over a 12-week treatment period, with a primary endpoint of improvement in average walking speed using the Timed 25 Foot Walk.

[125] From these descriptions of MS-F201 and MS-F202, the POSITA would derive the following information:

- Elan was supplying the fampridine SR composition;
- Doses of up to 25 mg bid were associated with statistically significant improvements in walking speed and leg muscle strength;
- Most of the improvement seen in the eight week MS-F201 trial was apparent at doses from 10 to 25 mg bid, and 9 of 25 subjects had improved walking speeds of more than 20% from baseline;
- The ongoing MS-F202 trial was comparing three fixed doses of 10, 15, and 20 mg bid over a treatment period of 12 weeks.

(2) Disclosure

[126] The main thrust of Biogen's novelty argument is that use claims, such as those at issue in the 277 Patent, are inextricably linked with their utility such that they are inventive because they convey "new knowledge to effect a desired result" (*Shell Oil Co v Commissioner of Patents*, [1982] 2 SCR 536 at 549). In this case, the claimed invention is the knowledge that 10 mg bid of fampridine SR results in a statistically significant and clinically meaningful improvement in walking in MS patients with walking disability. Disclosure of the MS-F202 protocol alone, without disclosure of its results, does not satisfy the disclosure requirement of the anticipation analysis.

[127] As construed, the resulting improvement in walking need not be clinically meaningful in the subjective sense. Following Biogen's line of argument, the claimed invention is therefore knowledge that 10 mg bid of fampridine SR results in a statistically significant improvement in walking in MS patients with walking disability.

[128] Biogen's disclosure argument is somewhat circular. If the claimed invention is as simple as the knowledge that the claimed use effects the claimed result, this knowledge was clearly disclosed in the Acorda S-1 by way of the MS-F201 trial results, which stated that doses of 10 mg bid to 25 mg bid were associated with statistically significant improvements in walking speed.

[129] Biogen downplays this result by highlighting that the improvement was only nominally significant when looking at the pooled data in terms of walking speed, rather than the pre-defined endpoint of walking time. In its submission, the POSITA would not understand that fixed doses of 10 mg bid improves walking, because the MS-F201 results used pooled data from an escalating dose study, and were not dose-specific. Further, the essential claim element of "at least two weeks" was not disclosed as part of the MS-F201 trial, and dependent claim element "every 12 hours" was not disclosed in the Acorda S-1 at all. On one hand, Biogen argues for a simplified claimed invention, and the other, it argues for a detailed parsing of the essential claim elements.

[130] The POSITA is taken to be trying to understand what the authors of the Acorda S-1 meant, reading the document for the purpose of understanding (*Sanofi* at para 25). While the evidence establishes that the POSITA would approach small studies such as the MS-F201 with a healthy dose of skepticism, there is no question that the POSITA would understand the reported MS-F201 results and the design and implementation of the MS-F202 study.

[131] As noted above, the disclosure requirement is satisfied if performing what is described in the prior art reference would necessarily result in infringement. The MS-F201 results disclose that the use of a fampridine SR composition at unit doses of 10 to 25 mg bid for treating a subject with MS is associated with a statistically significant improvement in walking. With the exception of the "time period of at least two weeks" element, all essential elements of claims 17, 18, 31, and 32 are disclosed.

[132] The MS-F202 study protocol, as included in the Acorda S-1, discloses the use of a fampridine SR composition at a unit dose of 10 mg bid for treating a subject with MS for a period of twelve weeks where the primary study endpoint is improvement in walking speed. The difficulty with the MS-F202 study protocol is that no results are included. The study protocol identifies each essential element of claims 17, 18, 31, and 32, and discloses that Acorda was conducting a study to see if the treatment worked. Therefore, the POSITA would not know whether using fixed doses of 10 mg bid results in a statistically significant improvement in walking speed.

[133] This is similar to the allegedly anticipatory art in *Hospira*. In that case, the "1994 Kennedy Report" disclosed the essential elements of at least some of the claims, stating that the patentee was conducting studies and results were not yet available. This Court found that the 1994 Kennedy Report, without results, did not anticipate the patent claims as it was speculative. Specifically, as no results were yet available, the "special advantage" of the adjunctive therapy at issue was not disclosed (as described in *Hospira*, above, at paras 67-70).

[134] The Federal Court of Appeal reversed, finding this analysis to be erroneous as it conflated the disclosure and enablement requirements of the test for anticipation. The relevant inquiry is whether the essential elements of each claim are disclosed, and each claim should be considered separately (*Hospira* at paras 71-72). The Federal Court of Appeal reiterated that the disclosure requirement is satisfied if performing what is described in the prior art reference would necessarily result in infringement, and noted that it failed to see how this requirement was not satisfied by the 1994 Kennedy Report, which disclosed the ongoing study and identified the likely utility of the proposed treatment (*Hospira* at paras 72-73). The matter of anticipation was remitted to the Federal Court for reconsideration.

[135] The Defendants rely on the Federal Court of Appeal's analysis for the principle that anticipation requires disclosure only of the essential elements of the claim in question, and disclosure of results are not required if they do not constitute essential elements of the claim (*Hospira* at paras 71-73). Biogen counters that *Hospira* does not stand for the general proposition that disclosure of a trial protocol anticipates a use claim that is supported by a clinical success.

[136] In my view, in this context the "result" at issue is not the MS-F202 trial results themselves, but rather the "result" that administration of 10 mg bid of fampridine SR provides a statistically significant improvement in walking speed for MS subjects in need of treatment. The 277 Patent teaches a use and a result. The MS-F202 study protocol teaches only the use, but the result at that point in time was uncertain. The distinction is subtle, but important.

[137] However, the POSITA reading the Acorda S-1—a single prior art reference—with a mind willing to understand, would have the benefit of both the MS-F202 study protocol and the MS-F201 study results. With the knowledge that doses of 10 to 25 mg bid were associated with a statistically significant improvement in walking speed, the POSITA would have a sound basis to further pursue fixed doses of 10, 15, and 20 mg bid as disclosed in the MS-F202 protocol. While the MS-F201 results appear to be pooled results using doses of 10 to 25 mg bid, the POSITA would understand Acorda S-1 to teach that use of any of these doses may be statistically significant. Therefore, as in *Hospira*, the prior art points the reader to precisely the kind of improvement that would occur with 10 mg bid dosing of fampridine SR: statistically significant improvements in walking speed.

[138] Despite the lack of results from the MS-F202 study, the disclosure requirement is satisfied if performing what is described in the prior art reference would necessarily result in infringement (*Sanofi* at para 25; *Hospira* at para 73). Performing the MS-F202 study protocol would necessarily result in infringement of the 277 Patent, and hence the disclosure requirement is satisfied for claims 17, 18, 31, and 32.

[139] Therefore, the Acorda S-1 discloses all essential elements of claims 17, 18, 31, and 32. While the Acorda S-1 discloses use of 10 mg bid, it does not specify the narrower claim limitation of dosing “every 12 hours” and accordingly an essential element of claims 23, 28, 37, and 42 is not disclosed.

(3) Enablement

[140] On the enablement requirement, Biogen argues that if the POSITA followed the MS-F202 protocol, including the predefined endpoint of the Timed 25 Foot Walk, the trial would fail, as the MS-F202 trial did. Only when applying the responder analysis would the POSITA obtain statistically significant results. Accordingly, the Acorda S-1 reference is not enabling.

[141] As highlighted by the Federal Court of Appeal in *Hospira*, what must be enabled are the essential elements of the claimed invention, not any particular experiments disclosed in the 277 Patent (*Hospira*, at para 74). Therefore, the focus must remain on the essential elements, rather than the POSITA's ability to perform the specific *post hoc* responder analysis detailed in the disclosure.

[142] I accept Biogen's argument that if the POSITA followed the MS-F202 protocol precisely, as per the pre-defined endpoint, the study would fail. However, at the enablement stage of the analysis, the POSITA is taken to be willing to conduct routine trial and error experiments to get the invention to work. Furthermore, the POSITA may consider the entirety of the prior art reference, and may use their common general knowledge to supplement the teachings in the prior art reference (*Sanofi* at para 37).

[143] In the Acorda S-1, the MS-F201 results show that subjects receiving placebo had slightly improved or worsened walking speeds, but none of the 11 subjects receiving placebo crossed the 20% improvement threshold. Conversely, 9 of the 25 subjects receiving fampridine SR twice per

day had improved walking speeds of greater than 20% from baseline. This information closely aligns with the POSITA's common general knowledge that due to the variability of MS, a given drug substance may provide significant improvement in one individual and have little to no effect in another. Further, the POSITA would know from the MS-F201 results that "doses of up 25 mg twice a day were well tolerated, and were associated with statistically significant improvements in walking speed."

[144] The POSITA would also have been aware of the prevalence of *post hoc* analyses and the possibility of conducting so-called "*n-of-1*" trials to sequentially dose patients with placebo and drug treatment to compare individual patients against themselves.

[145] Following the MS-F202 protocol, the POSITA would be able to perform the claimed invention without the exercise of inventive ingenuity or undue experimentation, even after discovering that the primary endpoint of improvement in average walking speed using the Timed 25 Foot Walk had failed. Using their common general knowledge, the POSITA would be able to routinely identify a subgroup of subjects who experienced a statistically significant increase in walking speed when taking 10 mg bid of fampridine SR.

(4) Conclusion on Anticipation

[146] The MS-F201 results and MS-F202 clinical trial protocol contained in the Acorda S-1 both disclose and enable the POSITA to perform the invention claimed in claims 17, 18, 31, and 32 of the 277 Patent, namely the use of 10 mg bid of fampridine SR for improving walking or

increasing walking speed in a subject with MS in need thereof. These claims are therefore anticipated.

[147] Because the narrower claim limitation of dosing "every 12 hours" is not disclosed in the Acorda S-1, claims 23, 28, 37, and 42 are not anticipated.

B. *Obviousness*

[148] The four part obviousness framework was laid out by the Supreme Court of Canada in *Sanofi* at paragraph 67:

> i. Identify the notional "person skilled in the art" and the relevant common general knowledge of that person;
>
> ii. Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
>
> iii. Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed;
>
> iv. Viewed without any knowledge of the alleged invention as claimed, do those differences constitute steps which would have been obvious to the person skilled in the art or do they require any degree of invention?

[149] In pharmaceutical inventions such as this one, the "obvious to try" test is appropriate and the following non-exhaustive factors should be taken into account at the fourth step of the obviousness inquiry (*Sanofi* at paras 68-71):

> i. 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?

> ii. 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?
>
> iii. Is there a motive provided in the prior art to find the solution the patent addresses?
>
> iv. What was the actual course of conduct which culminated in the making of the invention?

[150] The Federal Court of Appeal has referred to the actual course of conduct factor as "an elaboration of the second factor" (*Bristol-Myers Squibb Canada Co v Teva Canada Ltd*, 2017 FCA 76 at para 44). I will consider the inventors' course of conduct as part of the "extent, nature and amount of effort required to achieve the invention."

[151] The POSITA and their common general knowledge have been defined above. Before identifying the inventive concept, I will address the state of the art at the relevant date.

(1) The State of the Art

[152] Pursuant to section 28.3 of the *Patent Act*, the claimed invention must not have been obvious to the POSITA on the claim date. Prior to the introduction of section 28.3 to the *Patent Act*, there was no statutory basis for obviousness. When section 28.3 came into force, it was generally recognized that citable prior art for obviousness was limited to that which would have been found by the POSITA in a reasonably diligent search, consistent with the state of the law prior to codification (*Janssen-Ortho Inc v Novopharm Ltd*, 2006 FC 1234 at para 109 [*Janssen-Ortho*]; *Hospira* at paras 83-85).

[153] However, the Federal Court of Appeal recently held that it is an error to exclude prior art from the obviousness analysis simply because it would not have been located in a reasonably diligent search. The concept of the reasonably diligent search may still be relevant in considering whether the uninventive POSITA would have thought to combine certain pieces of prior art to make the claimed invention (*Hospira* at para 86).

[154] Biogen submits that this interpretation runs contrary to the intent of section 28.3, and the Court should instead only consider art which the POSITA would have found upon a reasonably diligent search. The Federal Court of Appeal's decision in *Hospira* is both clear and binding on this Court. Prior art will not be excluded from the obviousness analysis solely because the POSITA would not have found it after a reasonably diligent search.

[155] Drs. Ebers and Leist introduced numerous references reporting use of fampridine as a potential MS treatment, starting in the early 1990's. Both experts agreed that in 2004, the POSITA would look to the most recent literature to understand the state of the art rather than earlier studies that may have been superseded.

(a) *Schwid 1997 and Hayes 2003*

[156] Both parties rely on Schwid 1997 and their experts' interpretation thereof. Schwid 1997 is a *Neurology* publication evaluating the efficacy of fampridine SR using quantitative measures of motor function in MS patients. The study was randomized, double-blind, placebo-controlled, and designed to compare placebo and doses of 17.5 mg bid fampridine SR in 10 patients. The fampridine SR was supplied by Elan.

[157] Schwid 1997 reports that an earlier double-blind, placebo-controlled study of fampridine SR in 161 patients over six weeks failed to show any improvement in EDSS score as compared to placebo. The parties agree that this was the study conducted by Elan in 1994. The authors note, however, that EDSS may have been an inadequate outcome measure due to substantial intra-rater and inter-rater variability and the relative insensitivity of EDSS to change. Therefore, the authors sought to explore more sensitive, quantitative outcome measures of function in MS.

[158] The results section states that in the Schwid 1997 study, 9 of 10 patients walked more quickly on fampridine SR. The authors noted that treatment appeared particularly efficacious at serum levels above 60 ng/mL, but also noted that an earlier study had reported no difference in fampridine effects when testing eight patients at both high and low serum levels.

[159] The parties disagree on how the POSITA would interpret Schwid 1997. While both Drs. Ebers and Leist disparaged the study as underpowered due to the small number of subjects, and outdated as of 2004, Biogen argues that the key teaching to the POSITA is that there appeared to be an efficacy threshold for plasma concentrations of fampridine SR at about 60 ng/mL. Later publications repeated this suggestion of efficacy at higher plasma concentrations, citing back to Schwid 1997.

[160] A later publication reporting the pharmacokinetic properties of Elan's fampridine SR composition—Hayes 2003—reported that doses of 25 mg bid resulted in average steady state plasma concentrations of approximately 53 ng/mL. Therefore, in Biogen's submission, a POSITA looking to maintain fampridine plasma concentrations above the 60 ng/mL threshold

would expect doses of at least 30 mg bid of the Elan fampridine SR composition would be required.

[161] The Defendants submit this is a misdirection, and the key teaching of Schwid 1997 is that 9 of 10 patients walked more quickly taking 17.5 mg bid fampridine SR in a double-blind, placebo-controlled study. Expanding on this, the POSITA would recognize that Hayes 2003 reported doses of 17.5 mg bid resulted in average steady state plasma concentrations of approximately 35 ng/mL; far lower than the supposed threshold of 60 ng/mL.

(b) *The Goodman References*

[162] The Goodman Abstracts report the results of the MS-F201 study, stating that the fampridine SR group showed statistically significant improvement in walking speed from baseline compared to placebo, and dose response curves showed increasing benefit in the 10 to 25 mg bid range. The Abstracts also report that doses above 25 mg bid added little benefit and increased adverse effects. The parties agree that the Goodman Abstracts were publicly available prior to April 2004.

[163] The Goodman Poster is a poster presented by Dr. Andrew Goodman at a neurology conference in Baltimore in 2002. Dr. Goodman worked with the named inventors on clinical trials with fampridine SR. Biogen submits that Dr. Goodman only presented his poster for a short period of time, and it would fall outside the scope of a reasonably diligent search (*Janssen-Ortho*, above, at paras 57-58).

[164] As noted above, on the basis of *Hospira*, the Goodman Poster will not be excluded merely because it would not have been found by the POSITA upon a reasonably diligent search. The only outstanding issue is the scope of what was presented by Dr. Goodman in 2002. The Defendants presented three lines of argument establishing that the specific poster presented to the Court and relied on by the experts is in fact the same poster presented by Dr. Goodman in Baltimore in 2002. I find all of them compelling, and am satisfied that the Goodman Poster presented at trial accurately represents the information presented in Baltimore in 2002, and forms part of the state of the art for the purposes of the obviousness analysis.

[165] The Goodman Poster also reports the results of the MS-F201 study, and includes much of the same information contained in the Goodman Abstracts and the Acorda S-1. In addition to the information found in other pieces of prior art, the Goodman Poster discloses:

> • The MS-F201 study protocol specified that fampridine SR was to be taken every 12 hours;
>
> • The "Dose Response 25 ft. Walk" graphic shows an apparent decrease in time to walk 25 feet comparing off-drug walking time and on-drug walking time when subjects were taking 10 to 40 mg bid fampridine SR;
>
> • The average improvement in walking speed during the low dose period (10 to 25 mg bid) included greater than 20% increase for 9 of the 25 subjects;
>
> • In the "Conclusions" section, the poster reports that MS-F201 showed evidence of dose-response in the 20 to 40 mg/day range (10 to 20 mg bid), and there was little added benefit, and increased adverse effects, at doses above 50 mg/day (25 mg bid).

[166] The Defendants have established that the information in the Acorda S-1 was publicly available prior to the claim date, and this reference therefore forms part of the state of the art.

[167] Biogen submits that while Dr. Ebers based much of his obviousness opinion in his report on the Goodman Abstracts, Goodman Poster, and Acorda S-1 document, his true opinion on these pieces of art was revealed on cross-examination. There, he said that the data from the MS-F201 study does not have much power of persuasion, and the POSITA would look at the results with caution, particularly in light of the pooled data, small sample size (25 subjects on drug), and limited placebo arm (11 subjects). In Biogen's view, these admissions are consistent with Dr. Leist's position in his report and on cross-examination that the POSITA would see little value in the MS-F201 results.

[168] The Defendants took exception to Dr. Leist's reticence to answer questions on cross-examination, and the overly critical standard that he had the POSITA apply to the prior art, particularly the Goodman Poster. In the Defendants' submission, Dr. Leist approached the prior art seeking out failure.

[169] For the reasons given in the Expert Witnesses section above, the Court gives very little weight to Drs. Leist and Ebers' expert opinion evidence on obviousness, particularly as to how the POSITA would interpret and understand the prior art. This leaves the Court in the somewhat unusual position of interpreting the prior art through the eyes of the POSITA, while rejecting much of the expert evidence given at trial by both parties' expert neurologists.

[170] The Court accepts the conclusions made by Dr. Goodman, an undisputedly respected MS researcher, in his poster and abstracts. While the evidence of Drs. Leist and Ebers at trial shows that MS researchers, particularly those with a long history in the field, are highly skeptical of

new treatments that are not backed by double-blind, placebo-controlled studies, the prior art should be approached by a motivated POSITA with a mind willing to understand, not one myopically focused on seeking out failure. As stated by Justice Hughes with respect to prior disclosures in the anticipation context, prior art should be given the same, purposive interpretation as the claims at issue (*Shire Biochem Inc v Canada (Health)*, 2008 FC 538 at paras 64-65; see also *Sanofi* at para 25).

[171] Having considered the POSITA with a mind willing to understand, I would find that the state of the art at the relevant date included the following information:

i. A 1994 study of Elan's fampridine SR composition in subjects with MS using EDSS as the primary endpoint had failed (Schwid 1997);

ii. A randomized, double-blind, placebo-controlled study of 17.5 mg bid fampridine SR, using Elan's fampridine SR composition, found that 9 of 10 patients walked more quickly on fampridine SR (Schwid 1997);

iii. The placebo-controlled, double-blind MS-F201 study reported dose response in the 10 to 20 mg bid range, and 9 of 25 subjects experienced increases in walking speed of greater than 20% during the low dose period of 10 to 25 mg bid. Little added benefit and increased adverse events were seen above 25 mg bid (Goodman references, Acorda S-1).

iv. The Elan fampridine SR composition had the following pharmacokinetic properties after multiple dose administration (Hayes 2003):

	10 mg bid	**15 mg bid**	**20 mg bid**	**25 mg bid**
CavSS (ng/mL)	20.8 ± 5.7	31.0 ± 7.2	39.4 ± 9.3	53.3 ± 14.5
Tmax (h)	2.7 ± 1.0	3.2 ± 0.9	3.1 ± 1.2	2.6 ± 0.9

v. The MS-F202 study comparing fixed doses of fampridine SR at 10, 15, and 20 mg bid for 12 weeks with approximately 200 subjects was ongoing (Acorda S-1).

(2) The Inventive Concept

[172] The parties appear to agree that the inventive concept corresponds to the claims as construed. While I have found that claims 17, 18, 31, and 32 are anticipated by the Acorda S-1 reference, because the parties fully argued the issue of obviousness I will consider all of the Asserted Claims.

[173] As construed, all of the Asserted Claims include the inventive concept that 10 mg bid of fampridine SR improves walking or increases walking speed in MS patients in need thereof in a statistically significant way.

[174] Biogen submits that claims 19, 24, 33, and 38 and dependent claims include the added inventive concept that fampridine plasma concentrations of 15 to 35 ng/mL induce the desired improvement in walking or increase in walking speed.

[175] Dependent claims 21, 26, 35, and 40, as construed, include the further limitation that the fampridine SR composition provides a mean T_{max} in a range of 2 to 5 hours after administration.

[176] Dependent claims 23, 28, 37, and 42, as construed, include the limitation that the fampridine SR composition is in a form for administration every 12 hours.

(3) What differences exist between the state of the art and the inventive concept?

[177] Biogen submits that in 2004, the POSITA did not know what dose of fampridine SR would effectively improve walking or increase walking speed in subjects with MS with walking disability. Therefore, the difference between the state of the art and the inventive concept of the claims is that fampridine SR, taken in fixed doses of 10 mg bid, provides a statistically significant improvement in walking or walking speed in MS patients with walking disability.

[178] Biogen does not appear to take the position that the T_{max} claims or the "administration every 12 hours" claims add anything new that was not disclosed in the art. To this point, the Goodman Poster discloses that the MS-F201 study used dosing every 12 hours, and Hayes 2003 disclosed that the T_{max} for the Elan fampridine SR composition was approximately 3 hours.

[179] I accept that while the results of MS-F201 as disclosed in the Goodman references and the Acorda S-1 reported dose response and statistically significant improvements in walking speed in the 10 to 25 mg bid range, the prior art did not disclose that fixed doses of 10 mg bid fampridine SR taken "for a time period of at least two weeks" would improve walking or increase walking speed in MS subjects with walking disability in a statistically significant way.

[180] As reported in Hayes 2003, the C_{avSS} for 10 mg bid of the Elan fampridine SR composition is approximately 21 ng/mL. To the extent that the results of MS-F201 were based on pooled results from an escalating dose study, the POSITA would not have known the exact

range of fampridine SR plasma concentrations that induced a statistically significant improvement in walking or increase in walking speed.

> (4) Viewed without any knowledge of the alleged invention, do those differences constitute steps which would have been obvious to the POSITA, or do they require any degree of invention?

[181] Considering the obvious to try factors set out by the Supreme Court of Canada in *Sanofi*, I am satisfied that these differences would have been obvious to the POSITA at the relevant date.

[182] On the first factor, it is more or less self-evident that trying a low dose of fampridine SR twice daily would work. The Goodman Poster and Acorda S-1 reported statistically significant increases in walking speed using pooled data with doses from 10 to 25 mg bid, and the Goodman Poster reported dose response in the range of 10 to 20 mg bid. Based on the results of MS-F201 and the MS-F202 study protocol, the POSITA would have focused on fixed doses of 10, 15, and 20 mg bid, and would have only needed to conduct a small trial comparing these doses over a time period of over two weeks to confirm efficacy. In looking at the most recent developments in the state of the art, the POSITA would have focused on these three, identified, predictable solutions.

[183] Biogen submits that had the POSITA approached the problem, they would have done a dose escalation study in light of the common “start low, go slow” approach used for fampridine due to the possibility of adverse effects at higher doses. However, the POSITA reading the Acorda S-1 would know that doses of 10 to 25 mg bid showed statistically significant improvement in walking, and the ongoing MS-F202 study was already investigating fixed doses

of 10, 15, and 20 mg bid. The POSITA would have no need to escalate the dose with the knowledge that low doses provided the desired result.

[184] Biogen further submits that the POSITA would have focused on the common general knowledge that fampridine has a narrow therapeutic window, with increased adverse events observed above 25 mg bid fampridine SR. Further, several pieces of art reported fampridine's alleged efficacious plasma concentration threshold of 60 ng/mL. Therefore, in light of Hayes 2003, the POSITA would have known that 30 mg bid was required to achieve C_{avSS} over 60 ng/mL, and 20 mg bid was required to reach an average C_{max} of 60 ng/mL.

[185] This position can and should be rejected for multiple reasons. First, Schwid 1997 reported that "treatment appeared particularly efficacious in subject who achieved serum levels above 60 ng/mL." This is far from an absolute statement, and does not support Dr. Leist's opinion that the art discloses a "general view" that fampridine plasma concentrations over 60 ng/mL are necessary to provide therapeutic effect.

[186] Second, the experts agreed that the POSITA's knowledge would evolve over time, and they would look to more recent publications over outdated information. The most recent available information was from the Goodman references and the Acorda S-1 document, reporting that lower doses of fampridine SR—in the 10 to 25 mg bid range—provide statistically significant increases in walking speed. The 2003 Hayes Journal of Clinical Pharmacology reference relied on by Biogen was a study investigating the pharmacokinetics of single doses of

immediate release fampridine. While the paper refers to a possible 60 ng/mL efficacy threshold, this reported threshold simply cites back to Schwid 1997.

[187] Moreover, it is inconsistent for Biogen to argue that it was common general knowledge that doses above about 25 mg bid were toxic, as reported in the Goodman references, but suggest that the POSITA would nevertheless pursue fampridine SR doses of up to 30 mg bid in order to achieve plasma concentrations over 60 ng/mL. In light of the most recent teachings in the Goodman references, the POSITA would know that dose response could be achieved in the 10 to 20 mg bid range, and doses above 25 mg bid had little added benefit, and increased adverse events. To the extent that this teaching was not explicitly stated in the Acorda S-1, I am satisfied that the POSITA would have located the Goodman Abstracts in a reasonably diligent search.

[188] Biogen further submits that the 1994 Elan trial, which was reported in Schwid 1997, teaches away from the claimed invention. I do not accept Biogen's submission that the failed Elan study would have dissuaded the POSITA from even exploring the use of fampridine in MS patients. At the relevant date, this trial was approximately ten years old. Further, the authors of Schwid 1997 suggested that part of the reason for the study failure was that EDDS was an inadequately sensitive outcome measure. Based on the results of the small Schwid study, the POSITA would have focused on more sensitive quantitative outcome measures such as the Timed 25 Foot Walk, as the inventors of the 277 Patent did.

[189] On the second factor, given the state of the art in April 2004, the POSITA could have arrived at the claimed invention by carrying out routine trials. The MS-F201 results and the MS-

F202 study protocol provide the POSITA with a clear direction to pursue, and carrying out a similar study would have led to the realization that fixed doses of 10 mg bid provide a statistically significant improvement and increase in walking speed for some MS subjects with walking disability.

[190] The parties agree that the inventors' actual course of conduct is a relevant consideration in the obvious to try analysis, but disagree on the significance of the *post hoc* responder analysis conducted by the inventors of the 277 Patent. Biogen acknowledges that the responder analysis does not form part of the inventive concept, but maintains that no invention would have been realized without applying a *post hoc* consistency of response analysis to the clinical trial results. The Defendants acknowledge that the inventors' course of conduct is relevant, but insist that the focus of the obviousness analysis must remain on the claimed invention, rather than the means by which the invention was realized (*Apotex Inc v Pfizer Canada Inc*, 2019 FCA 16 at para 48).

[191] As construed, the POSITA would understand that a subject with MS in need of treatment is a subject with an EDSS score of approximately 3.5 to 7. However, as is clear from the results of the *post hoc* responder analysis reported in Example 5 of the disclosure, fampridine SR only provides a statistically significant improvement in walking for approximately one third of subjects with MS in need of treatment. Therefore, the invention that the POSITA is working towards is the discovery that 10 mg bid fampridine SR improves walking for some MS subjects with walking disability. As discussed above with respect to enablement, the POSITA would be able to routinely identify a subgroup of subjects who experienced a statistically significant

increase in walking speed when taking 10 mg bid fampridine SR. The method by which the POSITA identifies this subgroup is not claimed, and does not form part of the invention.

[192] Once the POSITA arrived at the claimed dosing regimen of 10 mg bid fampridine SR, there is nothing inventive about identifying the approximate plasma concentrations that result from this dosing regimen. Indeed, the C_{avSS} for 10 mg bid of Elan's fampridine SR composition was reported in Hayes 2003 to be approximately 21 ng/mL. The resulting fampridine plasma concentrations when dosing the Elan composition at 10 mg bid are merely inherent properties of the formulation itself. The allegedly inventive step is the knowledge that this low dose results in a statistically significant improvement in walking or increase in walking speed for some MS subjects with walking disability. Because this step is not inventive in light of the state of the art and the POSITA's common general knowledge, neither are the corresponding pharmacokinetic properties of the fampridine SR composition.

[193] Following the Federal Court of Appeal's guidance in *Hospira* that it may be relevant to consider the likelihood that a prior art reference would not have been located by the POSITA at this stage of the obviousness analysis, I am satisfied that the POSITA would have combined the pharmacokinetic parameters taught in Hayes 2003 with the fixed doses of 10 mg bid taught in the Acorda S-1. Both references report information on the Elan fampridine SR composition, and the Acorda S-1 states that the pharmacokinetic characteristics of fampridine SR in subjects with MS had been established in earlier trials sponsored by Elan.

[194] With respect to a motive in the prior art to find the solution taught in the patent, Dr. Ebers opined that as early as 1993, researchers had suggested that a fampridine SR formulation would have benefits to MS patients, and Schwid 1997 taught that 17.5 mg bid doses of fampridine SR resulted in improvement in walking for 9 of 10 patients. Therefore, the POSITA would have been motivated to pursue twice daily low doses of fampridine SR to improve walking in MS patients.

[195] Conversely, Dr. Leist opined that the POSITA would not have been motivated to conduct a study such as that described in Example 5 of the 277 Patent, and the POSITA specifically would not have had any motivation to conduct the *post hoc* responder analysis. As previously noted, the *post hoc* responder analysis does not comprise part of the claimed invention, and to the extent Dr. Leist incorporates it into his obviousness analysis, he focuses on the wrong question. The focus of the obviousness analysis is the claimed invention, which is defined by the essential elements of the claim. The claims do not contemplate any particular experiments or methods, and do not require that the POSITA be capable of carrying out the *post hoc* responder analysis relied on by Dr. Leist (*Hospira* at para 94).

[196] While Biogen somewhat distanced itself from Dr. Leist's infusion of the *post hoc* responder analysis into the inventive concept, I accept the Defendants' submission that the responder analysis, which is not claimed, cannot be used to make uninventive claims inventive. Importation of an unclaimed, allegedly inventive step from the disclosure into the plain language of the claims runs contrary to purposive construction of claims that are unequivocal and complete on their face (*BVD Company v Canadian Celanese Ltd*, [1937] SCR 221 at 237).

[197] As a final comment on the *post hoc* responder analysis, through the course of the trial Biogen repeatedly referred to the "forced" divisional application that resulted from the Commissioner's unity of invention objection. As previously noted, this is an overstatement, and the election to proceed with the use claims and file a divisional for the method claims was voluntary. Nevertheless, Biogen submits that patentees are not to be prejudiced by forced divisional applications, relying on the following passage from the Supreme Court of Canada's decision in *Consolboard Inc v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504 at 536-537:

> As I noted earlier, the appellant originally filed a single patent application for letters patent, but was required by the Commissioner of Patents to divide his application into two parts. It may be open to question whether the Commissioner of Patents should have split off the wafers and treated them as the subject of a separate patent but in my view a patentee is not to be prejudiced by enforced divisional applications.
>
> [Emphasis added]

[198] Biogen's reliance on this passage as a general proposition that patentees shall not be prejudiced by divisional applications is misguided. The relevant issue to the discussion of divisional applications in *Consolboard* was double patenting. MacMillan Bloedel sought to invalidate the second patent, which resulted from the divisional application, on the grounds that it was identical to the first. It was against this backdrop that Justice Dickson made the comments in the previous paragraph. Immediately following these comments, he stated:

> If patents are granted on divisional applications directed by the Patent Office, none of them should be deemed invalid, or open to attack, by reason only of the grant of the original patent.

[199] The principle to be taken from *Consolboard* is that patents granted on divisional applications are not open to attack by reason only of the grant of the original patent. The 277

Patent is the "original patent" in this case, and the double patenting principle from *Consolboard* does not apply.

(5) Conclusion on Obviousness

[200] To conclude, all Asserted Claims of the 277 Patent are invalid for obviousness. As of April 2004, the POSITA would have routinely bridged the gap between the state of the art and the inventive concept of the Asserted Claims. The POSITA would have understood that 10 mg bid dosing of fampridine SR was therapeutically effective to improve walking and increase walking speed for at least some patients with MS, and would have routinely verified this understanding by studying fixed doses of 10 mg bid fampridine SR. Specifying dosing every 12 hours, rather than twice a day, is not inventive. The claimed pharmacokinetic parameters—C_{avSS} and T_{max}—are inherent properties of the Elan formulation when administered at doses of 10 mg bid. Because it was not inventive to use doses of 10 mg bid, it was not inventive to claim the resulting plasma concentrations, which were known in the art.

[201] As a final comment on the expert evidence, Dr. Ebers was highly critical of the prior art and the alleged invention disclosed in the 277 Patent, seeing nothing inventive in the claims themselves. Dr. Leist was highly critical of the prior art, including the inventors' work leading up to the MS-F202 trial, but nevertheless saw inventiveness in the 277 Patent claims based on the responder analysis that led to the claimed invention. The fallacy in Dr. Leist's opinion evidence is that the *post hoc* responder analysis is not claimed, and cannot be used to elevate uninventive claims to the level of inventiveness.

C. *Methods of Medical Treatment*

[202] Patent claims to methods of medical treatment are prohibited in Canada (*Tennessee Eastman Co et al v Commissioner of Patents*, [1974] SCR 111 [*Tennessee Eastman*]; *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77 at paras 48-50). The Defendants allege that all of the Asserted Claims cover methods of medical treatment, and are therefore not patentable under section 2 of the *Patent Act*.

[203] The Defendants' submissions are based on analogies to two cases where claims were held to be invalid for claiming "how and when" a drug is to be used. In *Janssen Inc v Mylan Pharmaceuticals ULC*, 2010 FC 1123 [*Mylan*], this Court held claims to the use of galantamine invalid as unpatentable subject matter, noting that *Tennessee Eastman* remains good law in Canada because the policy concerns recognized in the case remain valid:

> Quite apart from the problem of "evergreening", the rationale for excluding such patents is that, for ethical and public health reasons, physicians should not be prevented or restricted from applying their best skill and judgment for fear of infringing a patent covering a pure form of medical treatment (as distinct from a vendible medical or pharmaceutical product). This is a particularly obvious concern in a case like this where the '950 Patent effectively blocks the use of a known compound (galantamine) for an established purpose (treating Alzheimer's disease) using a well-known treatment methodology (titration).
>
> [Para 53, emphasis added]

[204] The Defendants submit there is precious little to distinguish the Asserted Claims from those in *Mylan*. The 277 Patent effectively blocks the use of a known compound (fampridine SR) for an established purpose (increasing walking speed in MS patients) using a well-known

treatment methodology (twice daily dosing for at least two weeks). Therefore, based on the policy concerns recognized in *Tennessee Eastman* as articulated by the Court in *Mylan*, the 277 Patent claims are invalid because they prevent or restrict physicians from applying their skill and judgment.

[205] I note that because the Court in *Mylan* concluded that the claims covered unpatentable subject matter, it did not go on to fully address the other substantive issues in the application. However, with respect to the alleged obviousness of the patent claims, the Court noted:

> Suffice it to say that I have no doubt whatsoever that Janssen's claim to have discovered that the slow titration of galantamine reduced patient side-effects was well-known in the prior art and therefore would have been obvious to a person of skill at the relevant time.

[206] In my view, this approach better captures the situation at play in the present case. I agree with the Defendants that the 277 Patent claims the use of a known compound for an established purpose using a known treatment methodology. However, these general facts formed the basis of the obviousness finding, above. I do not agree that they also ground a separate finding of invalidity on the basis of unpatentable subject matter.

[207] The Defendants also rely on *Novartis Pharmaceuticals Canada Inc v Cobalt Pharmaceuticals Company*, 2013 FC 985 [*Novartis*], aff'd 2014 FCA 17 [*Novartis FCA*]. The claims at issue generally related to the once-a-year use of 5 mg of zoledronic acid to treat osteoporosis. This Court concluded that because each claim included treatment by intermittent dosages at certain intervals, the claims included "that which lies within the skill of the medical practitioner" and were therefore invalid (*Novartis*, above, at para 99). Notably, the Court

disregarded the “artificial nature” of the Swiss-type claims, and construed all of the claims at issue as use claims (*Novartis* at para 101).

[208] The Federal Court of Appeal summarily dismissed the appeal, finding that in order to allow the appeal, it would be necessary to conclude in the face of *Tennessee Eastman* that a method of medical treatment is patentable subject matter, or conclude that the Federal Court had misconstrued the patent (*Novartis FCA*, above, at paras 2-3).

[209] The Defendants generally assert that all of the Asserted Claims of the 277 Patent cover “how and when” fampridine SR tablets are to be administered, and are therefore invalid by analogy to *Novartis*.

[210] Conversely, Biogen submits the Defendants’ argument that the claims cover “how and when” fampridine SR is to be administered is no different from the Commissioner’s failed line of argument in *AbbVie Biotechnology Ltd v Canada (Attorney General)*, 2014 FC 1251 at paragraph 74. The Defendants adduced no evidence from any of the neurologists who gave evidence that they would be constrained in their practice by virtue of the 277 Patent.

[211] I agree with Biogen, and do not accept the Defendants’ argument that *Mylan* and *Novartis* stand for a general proposition that any patent claim to “how and when” a drug is administered covers unpatentable subject matter. While the Defendants also argue that *Hospira* suggests that merely characterizing something as a “vendible product” does not mean that the patent claims will not constrain a medical professional’s exercise of skill and judgment, I do not

read *Hospira* as making such a suggestion. In fact, the Federal Court of Appeal expressly stated that the claims at issue that were limited to fixed dosages and intervals of administration were claims for vendible products, and not invalid as methods of medical treatment (*Hospira* at para 53).

[212] In this case, all Asserted Claims are limited to fixed dosages and intervals of administration. Following the Federal Court of Appeal's approach in *Hospira*, the Asserted Claims are therefore not invalid as methods of medical treatment.

[213] Moreover, the Swiss-type claims relate to use in the manufacture of a medicament, and cover the actions of pharmaceutical manufacturers. The Defendants made no argument to the contrary, but submit that the Swiss-type claims nonetheless constrain "how and when" fampridine SR is to be administered, impinging on the physician's decision-making. Because the Defendants do not argue for the Court to construe the Swiss-type claims other than covering the activities of a pharmaceutical manufacturer, I fail to see how the Swiss-type claims could constrain medical professionals' exercise of skill and judgment.

[214] None of the Asserted Claims are invalid solely on the basis that they cover unpatentable methods of medical treatment.

VIII. Infringement by Taro

[215] Only infringement by Taro is at issue in this proceeding. Because I have found all Asserted Claims of the 277 Patent to be invalid, consideration of infringement is unnecessary. However, a brief comment on the parties' infringement submissions is warranted.

[216] Biogen bears the burden of proving infringement (*Monsanto Canada Inc v Schmeiser*, 2004 SCC 34 at para 29). However, as Taro admitted on discovery, it relies only on invalidity of the Asserted Claims as a basis for non-infringement in its NOA and Statement of Defence. As such, there is no basis for the Court to go on to consider whether or not Taro's proposed activities under its ANDS would otherwise constitute grounds for non-infringement. I agree with Biogen that if the claims were valid, Taro could not rely on legal argument to back away from its pleadings and admission on discovery.

[217] In any event, based on Taro's product monograph and the infringement evidence of Drs. Oh and Williams, Biogen has established on a balance of probabilities that if the 277 Patent claims were valid, Taro would take all essential elements of claims 18, 24, 26, 28, 32, 38, 40, and 42 if it made, constructed, used, or sold Taro-Fampridine in accordance with its ANDS.

IX. Conclusion

[218] In conclusion, the Acorda S-1 reference anticipates claims 17, 18, 31, and 32, and all Asserted Claims of the 277 Patent are invalid for obviousness.

[219] None of the Asserted Claims cover unpatentable methods of medical treatment.

X. Costs

[220] Pursuant to section 6.12 of the *Regulations*, the Court may make any order in respect of costs in accordance with the *Federal Courts Rules*, SOR/98-106. Amongst other factors, the Court may consider the diligence with which the parties have pursued the action and the extent to which they have reasonably cooperated in expediting the action.

[221] The parties agree that in complex pharmaceutical patent litigation between sophisticated parties such as these, costs in accordance with the Tariff are inadequate, and in this case, a lump sum representing 30% of incurred fees plus 100% of reasonable disbursements is appropriate.

[222] The Defendants also request increased costs to reflect the waste of fees and expenses the Defendants incurred in proving when the Acorda S-1 reference became available to the public. Specifically, the Defendants seek to recover all fees and disbursements associated with Dr. Kealey's expert evidence.

[223] Pursuant to Rule 400, the Court may consider, amongst other factors, any conduct of a party that tended to unnecessarily lengthen the duration of the proceeding, the failure of a party to admit something that should have been admitted, and whether the expense of having an expert witness give evidence was justified.

[224] I agree with the Defendants. Biogen did not seriously dispute Dr. Kealey's evidence, merely seeking to undermine his methodology on cross-examination. Further, Dr. Cohen's evidence corroborated the public nature of the Acorda S-1 document; Acorda submitted the document in order to raise capital on public markets in September 2003. There is no question that this document was available to the public before the relevant date of April 2004.

[225] I therefore exercise my discretion to award the Defendants all legal costs and the entirety of the disbursements associated with the preparation of Dr. Kealey's expert report and testimony. These costs should be assessed separately from the remainder of the Defendants' reasonably incurred legal fees and disbursements, to which they are entitled to a lump sum award of 30% of actual legal fees reasonably incurred plus 100% of reasonable disbursements. The Defendants represent that they jointly incurred approximately $1 million in legal fees, and $200,000 in reasonable disbursements, and are therefore entitled to a lump sum of approximately $500,000.

[226] Biogen submits that the Defendants should not be permitted to recover for any fees or disbursements that are the result of work that was duplicative. To this end, Taro and Pharmascience's NOAs and Statements of Defence were essentially identical, and the Defendants used the same experts for issues of validity, having these experts sign only a Taro Code of Conduct. Further, the Defendants conducted joint examinations at trial, made common written and oral arguments, and exchanged joint requests and responses to requests to admit.

[227] Based on the parties' costs submissions, it is not clear whether any of the Defendants' fees and disbursements are in fact duplicative. Unless Biogen directs the Court to fees or

disbursements that the Defendants have double counted, the quantum of costs will be as represented by the Defendants, with appropriate adjustment for fees and disbursements related to Dr. Kealey's evidence.

[228] A copy of this judgment and reasons shall be placed on each of Court files T-1163-18 and T-220-19.

JUDGMENT in T-1163-18 and T-220-19

THIS COURT'S JUDGMENT is that

1. Biogen's actions are dismissed;
2. The Acorda S-1 reference anticipates claims 17, 18, 31, and 32 of the 277 Patent, and all Asserted Claims of the 277 Patent are invalid for obviousness;
3. Costs to the Defendants, assessed as all fees and disbursements associated with Dr. Kealey's expert evidence, 30% of the remaining reasonably incurred legal fees, and 100% of remaining reasonable disbursements.

"Michael D. Manson"
Judge

APPENDIX A

Relevant Claims of the 277 Patent

Shaded claims are not asserted by Biogen, except to the extent that they are incorporated into dependent claims.

Claim No.	Claim Language
15	Use of a sustained release 4-aminopyridine composition for improving walking in a subject with multiple sclerosis in need thereof at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
16	Use of a sustained release 4-aminopyridine composition in the manufacture of a medicament for improving walking in a subject with multiple sclerosis in need thereof at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
17	Use of a sustained release 4-aminopyridine composition for improving walking in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
18	Use of a sustained release 4-aminopyridine composition in the manufacture of a medicament for improving walking in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
19	The use of claim 15 or 17, wherein the 4-aminopyridine composition exhibits a C_{avSS} of 15 ng/ml to 35 ng/ml.
20	The use of claim 15 or 17, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 1 to 6 hours after administration of the 4-aminopyridine composition to the subject.
21	The use of claim 15 or 17, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 2 to 5 hours after administration of the 4-aminopyridine composition to the subject.
22	The use of claim 15 or 17, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 2 to 6 hours after administration of the 4-aminopyridine composition to the subject.
23	The use of any one of claims 15, 17, and 19 to 22, wherein the 4-aminopyridine composition is in a form for administration every 12 hours.
24	The use of claim 16 or 18, wherein the medicament exhibits a C_{avSS} of 15 ng/ml to 35 ng/ml.
25	The use of claim 16 or 18, wherein the medicament provides a mean T_{max} in a range of 1 to 6 hours after administration of the medicament to the subject.
26	The use of claim 16 or 18, wherein the medicament provides a mean T_{max} in a range of 2 to 5 hours after administration of the medicament to the subject.
27	The use of claim 16 or 18, wherein the medicament provides a mean T_{max} in a range of 2 to 6 hours after administration of the medicament to the subject.
28	The use of any one of claims 16, 18, and 24 to 27, wherein the medicament is in a form for administration every 12 hours.
29	Use of a sustained release 4-aminopyridine composition for increasing walking speed in a subject with multiple sclerosis in need thereof at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
30	Use of a sustained release 4-aminopyridine composition in the manufacture of a medicament for increasing walking speed in a subject with multiple sclerosis in need thereof at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
31	Use of a sustained release 4-aminopyridine composition for increasing walking speed in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.

32	Use of a sustained release 4-aminopyridine composition in the manufacture of a medicament for increasing walking speed in a subject with multiple sclerosis in need thereof for a time period of at least two weeks at a unit dose of 10 milligrams of the 4-aminopyridine twice daily.
33	The use of claim 29 or 31, wherein the 4-aminopyridine composition exhibits a C_{avSS} of 15 ng/ml to 35 ng/ml.
34	The use of claim 29 or 31, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 1 to 6 hours after administration of the 4-aminopyridine composition to the subject.
35	The use of claim 29 or 31, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 2 to 5 hours after administration of the 4-aminopyridine composition to the subject.
36	The use of claim 29 or 31, wherein the 4-aminopyridine composition provides a mean T_{max} in a range of 2 to 6 hours after administration of the 4-aminopyridine composition to the subject.
37	The use of any one of claims 29, 31, and 33 to 36, wherein the 4-aminopyridine composition is in a form for administration every 12 hours.
38	The use of claim 30 or 32, wherein the medicament exhibits a C_{avSS} of 15 ng/ml to 35 ng/ml.
39	The use of claim 30 or 32, wherein the medicament provides a mean T_{max} in a range of 1 to 6 hours after administration of the medicament to the subject.
40	The use of claim 30 or 32, wherein the medicament provides a mean T_{max} in a range of 2 to 5 hours after administration of the medicament to the subject.
41	The use of claim 30 or 32, wherein the medicament provides a mean T_{max} in a range of 2 to 6 hours after administration of the medicament to the subject.
42	The use of any one of claims 30, 32, and 38 to 41, wherein the medicament is in a form for administration every 12 hours.

FEDERAL COURT

SOLICITORS OF RECORD

DOCKETS:	T-1163-18 AND T-220-19
DOCKET:	T-1163-18
STYLE OF CAUSE:	BIOGEN CANADA INC., BIOGEN INTERNATIONAL GMBH AND ACORDA THERAPEUTICS, INC v TARO PHARMACEUTICALS INC.
AND DOCKET:	T-220-19
STYLE OF CAUSE:	BIOGEN CANADA INC., BIOGEN INTERNATIONAL GMBH AND ACORDA THERAPEUTICS, INC v PHARMASCIENCE INC.
PLACE OF HEARING:	TORONTO, ONTARIO
DATE OF HEARING:	MARCH 2-6, 9, 10, 13, 2020
JUDGMENT AND REASONS:	MANSON J.
DATED:	MAY 15, 2020

APPEARANCES:

John Norman Alex Gloor Rebecca Stiles Adam Heckman	FOR THE PLAINTIFFS
Jonathan Stainsby Scott Beeser	FOR THE DEFENDANT TARO PHARMACEUTIALS INC.
Aleem Abdulla	FOR THE DEFENDANT PHARMASCIENCE INC.

SOLICITORS OF RECORD:

Gowling WLG (Canada) LLP Barristers and Solicitors Ottawa, Ontario	FOR THE PLAINTIFFS
Aitken Klee LLP Barristers and Solicitors Toronto, Ontario	FOR THE DEFENDANT TARO PHARMACEUTICALS INC.
Aitken Klee LLP Barristers and Solicitors Ottawa, Ontario	FOR THE DEFENDANT PHARMASCIENCE INC.