Federal Court of Appeal | Cour d'appel fédérale

Date: 20220808

Dockets: A-145-20
A-146-20

Citation: 2022 FCA 143

CORAM: **GAUTHIER J.A.**
GLEASON J.A.
RIVOALEN J.A.

Docket: A-145-20

BETWEEN:

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

Appellants

and

PHARMASCIENCE INC.

Respondent

Docket: A-146-20

AND BETWEEN:

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

Appellants

and

TARO PHARMACEUTICALS INC.

Respondent

Heard by online video conference hosted by the Registry on February 22, 2022.

Judgment delivered at Ottawa, Ontario, on August 8, 2022.

PUBLIC REASONS FOR JUDGMENT BY:	GAUTHIER J.A.
CONCURRED IN BY:	GLEASON J.A. RIVOALEN J.A.

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PUBLIC REASONS FOR JUDGMENT

This is a public version of confidential reasons for judgment issued to the parties. The two are identical, there being no confidential information disclosed in the confidential reasons.

GAUTHIER J.A.

[1] The appellants appeal from the decision of the Federal Court (*per* Manson J., 2020 FC 621) (the "FC Decision"). In its decision, the Federal Court dismissed the appellants' two patent infringement actions (in T-1163-18 and T-220-19) instituted pursuant to subsection 6(1) of the *Patented Medicines (Notice of Compliance) Regulations*, S.O.R./93-133 (the *Regulations*). The Federal Court concurrently heard both actions on issues of validity based on the same allegations and evidence along with the issue of infringement with respect to Taro Pharmaceutical Inc. (Taro), whose non-infringement claim was dependent on the validity issues. The FC Decision relates to the validity of Canadian patent number 2,562,277 (the 277 Patent) and Taro's alleged infringement of the 277 Patent in Court file T-1163-18. The infringement portion of the action against Pharmascience Inc. (Pharmascience) in T-220-19 was to be scheduled later, if necessary.

[2] The Federal Court concluded that a key document in this litigation anticipated four claims of the 277 Patent and that all of the asserted claims were invalid for obviousness. Having concluded that the invalidity of the asserted claims was the only ground on which Taro relied as

a basis for non-infringement in its Notice of Allegation (NOA) and Statement of Defence, the Federal Court did not address infringement further in its decision. This is the subject of a cross-appeal by Taro.

[3] Although there are some unusual facts in this matter, none of the issues raised before us involves any new questions of law. The main issue is whether, when applying the law, the Federal Court failed to adopt the perspective of a person skilled in the art (POSITA) when it construed the patent and reviewed the prior art. A subsidiary issue is whether the Federal Court should have dismissed the attack on the validity of the 277 Patent because the only expert evidence presented by the respondent was inadmissible and, thus, the respondents could not have met their burden of proof.

[4] For the reasons set out below, I have concluded that this appeal and the cross-appeal should be dismissed.

I. Background

[5] For ease of reading, I will provide a background about the patent at issue, the parties and the main witnesses whose evidence I will be discussing.

[6] The 277 Patent is entitled “Methods of Using Sustained Release Aminopyridine Compositions”. Although the 277 Patent contains 112 claims, the parties limited the issues before the Federal Court to independent claims 17, 18, 31, 32, and dependent claims 19, 21, 23, 24, 26, 28, 33, 35, 37, 38, 40, 42. All the claims in this patent deal with the use of a composition

of sustained release (SR) 4-aminopyridine (4-AP), also known as fampridine, to treat multiple sclerosis (MS) or the making of a medicament composed of such composition for such use (i.e., a Swiss-type claim).

[7] The description of the 277 Patent refers to some embodiments of the invention as being methods for selecting individuals based on responsiveness to a treatment, and deals at length with what is referred to as Example 5, which resulted from a *post hoc* analysis. However, it is no longer disputed that such methods including the *post hoc* responders analysis described in Example 5 are not part of the invention claimed in the 277 Patent. More will be said about this later on.

[8] The 277 Patent is owned by Acorda Therapeutics Inc. (Acorda), a Delaware corporation that is one of the appellants in this proceeding. The President and CEO of Acorda, Dr. Cohen, is one of the inventors named in the 277 Patent. He was a factual witness before the Federal Court (FC Decision at paras. 27-43). Acorda licences the 277 Patent to Biogen International GmbH (a Swiss corporation), who in turn authorized Biogen Canada to use and sell the invention claimed in the 277 Patent. Unless otherwise indicated, these entities are referred to collectively in these reasons as Biogen. Biogen Canada is an Ontario corporation related to Biogen International; it is a first person within the meaning of subsections 4(1) and 6(1) of the *Regulations*. It markets and sells FAMPYRA® in Canada, a sustained released (SR) composition of fampridine.

[9] The respondents, Taro and Pharmascience, are generic pharmaceutical companies incorporated under the laws of Ontario. They were seeking access to the Canadian market with

their own fampridine SR products. Both parties sent an NOA, pursuant to subsection 5(3) of the *Regulations,* before the appellants commenced their actions in accordance with the *Regulations*.

[10] Dr. Oh, a staff neurologist at St-Michaels Hospital and a scientist at the Keenan Research Center for Biomedical Science in Toronto, was qualified to give expert opinion evidence on various issues listed at paragraph 47 of the FC Decision. She gave evidence on the POSITA's common general knowledge and infringement of the 277 Patent by Taro based on her understanding of the asserted claims.

[11] Dr. Thomas Leist is the Chief of Clinical Neuroimmunology Division and Director of the Comprehensive Multiple Sclerosis Center at Thomas Jefferson University in Philadelphia, Pennsylvania. He gave evidence on the scientific background of MS, claim construction, state of the art and the POSITA's common general knowledge as of April 2004, anticipation and obviousness. He responded to Dr. Ebers' opinions on anticipation and obviousness. He was qualified by consent to give expert opinion evidence on the matters listed in paragraph 57 of the FC Decision.

[12] Dr. George Ebers is an *emeritus* professor at the Nuffield Department of Clinical Neurology at the University of Oxford. The description of his activities during the relevant period from 1997 to 1999, and to present are outlined in the FC Decision at paragraphs 62 to 64. He was qualified by consent to give expert opinion on matters set out in paragraph 65 of the FC Decision. He was the only expert presented by the respondents to deal with issues of claim construction, anticipation and obviousness.

II. The Federal Court Decision

[13] The Federal Court defined the POSITA to whom the 277 Patent is addressed as follows:

> [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.

[14] The Federal Court then described in some detail what was commonly known about MS by the POSITA. To avoid repetition, I will provide more detail about these findings later on in these reasons (see paras. 61-70 below). I will simply say here that such findings are not challenged by either party, and they were also properly grounded in the evidence before the Federal Court (FC Decision at paras. 8-17; 86-91).

[15] Turning to claim construction, the Federal Court started by reviewing the main terms requiring construction in the asserted claims, all of which are reproduced in Appendix A to the FC Decision. It is apparent from a review of the FC Decision that the Federal Court considered the description of the 277 Patent, the CGK, at least some of the expert evidence, and the actual language of the claims in reaching its conclusion on claim construction.

[16] The Federal Court found that the several terms in the claims in suit required construction. These included, among others, the terms “improving walking”, “a subject with MS in need thereof”, “for a time period of at least two weeks” and “unit dose of 10 milligrams of the

4-aminopyridine twice daily". At paragraph 94 of its decision, the Federal Court held that 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.

[17] In so holding, the Federal Court expressly rejected Dr. Leist's opinion that improved walking would be understood as including not only a quantitative improvement, but also as requiring as an essential element, a qualitative one based on a subjective perception of improvement by the MS patient (FC Decision at para. 95). The Federal Court also disagreed with Biogen's argument that a further claim limitation is included in some of the asserted claims based on Dr. Leist's opinion that "for a time period of at least two weeks" requires that the improvement in walking be consistently improved during at least two weeks. In the Federal Court's view, the plain claim language merely required use of 10 mg bid fampridine SR over the entire two-week period (FC Decision at para. 97).

[18] The Federal Court also construed the expression C_{avSS} based on the evidence of Dr. Ebers as meaning average plasma concentration at steady state (FC Decision at para. 100). This term required construction in respect of dependent claims 19, 24, 33, and 38.

[19] With respect to dependent claims 21, 26, 35 and 40, which introduce a further limitation in respect of "mean T_{max}" in a range 2 to 5 hours after administration, the Federal Court used the definition of T_{max} found in the disclosure (also referred to as the description); that is, the "time to maximum plasma concentration" (FC Decision at para. 101).

[20] There is no need to refer here to all the elements of each asserted claim. Rather, I will simply reproduce the summary of the essential elements as described in paragraphs 109, 110 and 111 of the FC Decision:

> [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.

[21] I understand that the two expressions "statistically significant way" and "in a subject with MS who experiences some form of walking disability" in subparagraphs 109(ii) and (iii) above are meant to be read together with the findings set out in paragraph 94 of the FC Decision (as reproduced in paragraph 16 above).

[22] The Federal Court then addressed the validity attacks after noting that the 277 Patent is presumed to be valid, and that the defendant bears the burden of establishing each ground of invalidity on the balance of probabilities (FC Decision at para. 112).

[23] After identifying the cut-off dates for citable prior art, the Federal Court first dealt with anticipation (FC Decision at paras. 114-147). Prior to trial, the parties provided the Federal Court with a joint statement of issues, where Taro asserted that it would rely only on the Acorda S-1 document with respect to anticipation. The Federal Court refused Taro's request in closing submissions to admit the Goodman Abstracts and Goodman Poster for the purposes of anticipation after it argued it had excluded these documents in error. There is no need to go into great detail about this finding here, given that I have come to the conclusion that this appeal can be determined without addressing this point.

[24] It is still useful to say a few words at this point about Acorda S-1, because it is referred to later in the FC Decision when dealing with obviousness. Acorda S-1 is a public financial document filed by Acorda with the US Securities and Exchange Commission (SEC) issued in the Fall of 2003. In this document, Acorda summarises its clinical studies respecting the use of fampridine SR, including studies referred to as MS-F201, which was completed in 2001, and MS-F202, initiated in early 2003, with results anticipated by the end of March 2004. These studies were conducted by Acorda in cooperation with Elan, an Irish pharmaceutical company that then owned at least one patent on fampridine (SR) for use in MS treatment cited by the experts (see also Patent Number 5,580,580, AB Vol. 2, at p. 490). Elan also supplied the SR composition to Acorda for the trials. It is worth reproducing paragraphs 123 to 125 of the FC Decision, which deal with this document in the context of its anticipation analysis:

> [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.

[25] Because the appellants argue that the Federal Court did not adopt the mantle of the POSITA, it is also worth reproducing paragraph 130 of the FC Decision:

> [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.

[26] Although I will not deal with anticipation , the Federal Court made a few comments under enablement that are relevant to its analysis of obviousness in that they include factual findings that pertain to both enablement and obviousness. In this regard, I believe it is both fair and necessary to read the Federal Court's reasons holistically (see also para. 191 of the FC Decision).

[27] For purposes of assessing enablement, the POSITA is taken to be willing to conduct routine trial and error experiments to get an invention to work. To do so, they may consider the entirety of the prior art reference (here the Acorda S-1) and may use their common general knowledge to supplement the teachings in the prior art reference (*Apotex Inc v. Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 (*Sanofi*) at para 37). At paragraphs 144 and 145 of its decision, the Federal Court explained why, in its view, the POSITA would have been able to get the invention to work, despite the fact that, by applying only the pre-defined endpoints, the MS-

F202 study would fail (one of the unusual facts in this matter). More particularly, the Federal Court found that 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 those patients with placebo and drug treatments to compare individual patients against themselves. In the Federal Court's view, 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.

[28] Finally, the Federal Court dealt with obviousness at paragraphs 148 to 201 of its decision. First, it correctly identified the obviousness framework laid out by the Supreme Court in *Sanofi*, and noted that it is appropriate to apply the "obvious to try" test in this case (which is not disputed). Then, it reviewed the state of the art at the relevant date (FC Decision at paras. 152-171) before identifying the inventive concept (FC Decision at paras. 172-176). This enabled the Federal Court to then address the difference between the state of the art and the inventive concept at paragraphs 177 to 179.

[29] At this stage, it is important to reproduce paragraphs 169 and 170 of the FC Decision that are at the heart of the appellants' argument that the Federal Court failed to read the prior art through the eyes of a POSITA.

> [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 *Sanof*i at para 25).

[30] In paragraphs 181 to 199 of the decision, the Federal Court addressed the question of whether the differences it had identified would require any degree of inventiveness and dealt with the main arguments presented by the parties. It is in this section that the Federal Court considered the inventors' course of action (FC Decision at paras. 190-191)—a factor that, according to the appellants, the Federal Court did not give sufficient weight to.

[31] It is also in this section that the Federal Court reiterated that the *post hoc* responder analysis discussed in Example 5 of the 277 Patent and certain parts of the description are not part of the claimed invention or the inventive concept, contrary to the position taken by Dr. Leist (see also para. 195 of the FC Decision). It also commented on the impact of the divisional application filed by Acorda in response to a Patent Office unity of invention objection. Originally, Acorda had included many method claims in its application to cover the responder analysis referred to in the description portion of the application (in particular see 277 Patent at paras. 0019-0020 at Example 5 and the various paragraphs referring to it or explaining it, such as paras. 0078-0079). The material dealing with such methods in the description was necessary to support the claims that were later removed and included in the divisional application.

[32] At paragraph 200 of its decision, the Federal Court concluded as follows in respect of 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.

[33] There is no need to discuss the Federal Court's finding under "Methods of Medical Treatment" as this was not an issue raised before us.

III. Issues and standards of review

[34] This appeal attracts the usual appellate standards of review set out in *Housen v. Nikolaisen*, 2002 SCC 33. However, the parties disagree as to the characterization of the questions raised by the appellants, and therefore as to the standard that would apply to them.

[35] In their memorandum, the appellants frame the issues as follows:

1. Did the Federal Court err in declaring the asserted claims to be invalid by failing to adopt the perspective of the POSITA when assessing the 277 Patent and the prior art for obviousness and anticipation?

2. Did the Federal Court err in failing to adopt a perspective of the POSITA in construing the claimed terms “improving walking” and “increasing walking speed”?

3. Did the Federal Court err in failing to find that the respondents failed to meet their evidentiary burden to prove that the 277 Patent is invalid?

[36] It is undisputed that in the absence of an extricable error of law, a trier of fact’s conclusions with respect to obviousness and anticipation are reviewed on the standard of palpable and overriding error. The appellants claim that there is an extricable error of law here. I note again, however, that the appellants do not dispute the applicable general principles of law and tests expressly stated by the Federal Court. Both parties recognized that the trial judge, who was an intellectual property (IP) practitioner before he became a leading Federal Court Judge in IP matters, was particularly well acquainted with them.

[37] Given that the issue here is really about an alleged misapplication of the principles rather than the principles themselves, an appellate court should normally intervene only where there is a palpable and overriding error. In that respect, the appellants maintain that if this characterization applies here, they have met their burden in any event.

[38] With respect to the construction of the claim terms referred to above, it is undisputed that the construction of the patent is a matter of law, subject to the correctness standard. That said, there is also no dispute that in respect of the appreciation of the expert evidence on how a POSITA would understand specific terms, the trier of fact is entitled to deference and the

standard of palpable and overriding error applies (*ABB Technology AG v. Hyundai Heavy Industries Co., Ltd.*, 2015 FCA 181 at paras 22-23).

[39] Considering that this Court is tasked with construing the language of the claims as a matter of law, it becomes irrelevant to determine whether, as also argued by the appellants; the Federal Court may have erred by considering validity and infringement in its purposive construction analysis at paragraph 96. I do not share the appellants' literal interpretation of this paragraph. As I mentioned in *Apotex Inc. v. Astrazeneca Canada Inc.*, 2017 FCA 9 (*Astrazeneca*) at paragraph 43, one must be particularly careful when assessing the submissions that a Court has paid lip service to the well-established principles it clearly meant to apply. This is an often-raised argument. As posited in *Astrazeneca*, are we to assume that because Justice Binnie discussed claims construction in the section of his reasons entitled infringement in *Whirlpool Corp. v. Camco Inc.*, 2000 SCC 67, (*Whirlpool*), he was misapplying the rules he had just set out in that very case?

[40] Turning to the third question, the appellants argue that the Federal Court made an extricable error of law by determining the issue of admissibility without a motion and detailed arguments on the issue. They say that the report of Dr. Ebers should have been held inadmissible and thus the validity attacks should have been dismissed as the respondents did not meet their burden of proof. They also argued that in any event, having decided to give no weight to the evidence of this expert witness, the Federal Court had to dismiss those attacks. I do not agree that according no weight to evidence is the same as according little weight to much of the evidence. This Court will not intervene in this respect in the absence of a palpable and overriding error.

[41] Because the issue of admissibility of Dr. Ebers' report can have an impact on all the issues in this appeal, I will deal with it first. I will then address the issue of claim construction followed by the two issues concerning obviousness, which, as will be seen, affects the validity of all the asserted claims. It is therefore not necessary to deal with anticipation of four of the claims to determine this appeal.

[42] Taro's cross-appeal also not need to be addressed in light of my conclusion in respect of the issues raised by the appellants.

IV. Analysis

[43] A few preliminary remarks are warranted. As already mentioned, this case, in my view, was particularly difficult in that it involved many unusual features, albeit not unique ones. I will refer only to a few here. First, the 277 Patent's description includes a substantial amount of information that is no longer directed at a subject matter claimed. This can easily lead astray expert witnesses who are not particularly familiar with patent law. Second, MS is not a typical disease because of the constant fluctuation of its symptoms, and the fact that only a portion of the individual patients in need of the subject matter claimed will effectively respond to the active ingredient (fampridine SR). This portion of patients cannot be ascertained prospectively, and it is not disputed that the claims as written are not referring only to the so-called "responders" in the description. Third, for various reasons, the expert evidence on both sides could not be given much weight and certainly not as much weight as the parties, particularly the appellants, would have liked.

[44] These factors and others contributed to this decision being factually complex. In circumstances like these, this Court must be very careful in not imposing its own view of the weight to be given to the evidence. This is simply not our role.

A. *The Admissibility of Dr. Ebers' Evidence*

[45] The appellants argue that the Federal Court erred by not declaring the whole of Dr. Ebers' report inadmissible. As mentioned, the appellants add that had it done so, the Federal Court would have had no choice but to dismiss the validity attacks by the respondents.

[46] The objection to the admissibility of this evidence is based on the fact that the section entitled "State of the art" in Dr. Ebers' report consisted mostly of paragraphs found in Taro's NOA dated May 3, 2018, a document he had never reviewed. As mentioned by the respondents during the trial, these are limited to quoting various extracts from the relevant prior art. There is no issue that all these papers were well-known to Dr. Ebers. In fact, the Federal Court noted that this witness dedicated much of his life to studying and documenting MS and treatments for the disease (FC Decision at para. 67).

[47] I agree with the appellants that an appellant is free to contest in the context of an appeal on the merits a trier of fact's finding made during the course of a trial in respect of admissibility of evidence. But this does not mean that such a right can be used as an ambush to preclude the opposing party from their right to present their case. There is a minimum duty of due diligence on a party who wishes to bring an admissibility objection to ensure that it is squarely made and properly determined, especially when it intends to have this objection reviewed on appeal.

[48] There is also a minimum level of diligence that a court can expect from a party, especially a sophisticated one like the appellants, who is represented by experienced counsel, as to the timing of such an objection. Admissibility of evidence from a party's sole expert can have a real prejudicial impact on the said party's rights and the way that party's counsel will conduct their cross-examination of other experts and construct their case.

[49] The Supreme Court of Canada has emphasized that admissibility of expert evidence should be scrutinized when the expert evidence is presented for acceptance to the Court so as to enable the trier of fact to exercise its role as a gatekeeper (see *R. v. J.-L.J.*, 2000 SCC 51 at para. 28). To ensure this, the *Federal Courts Rules* S.O.R./98-106 (the Rules) provide that objections as to admissibility must be raised in writing and as soon as possible in the proceeding (see Rule 52.5). In this case, at the trial management conference, the trial judge expressly directed that all preliminary issues and motions be brought to his attention before February 26, 2020. These normally would include any remaining objections to the experts and their reports.

[50] Here, the duplication contained in Dr. Ebers' report, on which the appellants' argument rests, should have been clearly evident to them as soon as they received his report, which also included his Code of Conduct for Expert Witnesses certificate mandated by the *Federal Courts Rules* outlining his obligations as an expert witness. By the time the appellants mentioned their concerns to the Federal Court on the second day of their cross-examination of Dr. Ebers, they had spent some time preparing a document, highlighting in yellow all the duplicated paragraphs in the report and NOA.

[51] At the hearing before us, the appellants claimed that it was not evident to them that this duplication was a problem because they had wrongly assumed that Dr. Ebers was involved in the drafting of Taro's NOA. They learned of their error in the course of Dr. Ebers' cross-examination after he had been qualified as an expert. However, a simple inquiry with opposing counsel would have revealed if there was a need to contest the issue by way of a motion as was directed by the Federal Court during the trial management conference for this action.

[52] Instead, the appellants' counsel came prepared to cross-examine Dr. Ebers with respect to this assumption (AB Vol. 32, at p. 9342-9343 of the transcript). Furthermore, after the first day of cross-examination, they had time to consider bringing a motion to challenge the admissibility of the report before the trial resumed the next day. Instead of doing so they had a minimal exchange with Justice Manson:

> MR. JUSTICE MANSON: Well, the fact it's there and the fact if you put that question to him, he is going to say whatever he says, and at the end of the day you're going to -- you are going to tell me it's verbatim what was in the Notice of Allegation, and then your point is made, I mean. And I will take whatever weight and whatever I want to give to that in terms of your question about impartiality. I get your point.
>
> MR.
>
> (Ebers cross, AB Vol. 32, Tab 79, p. 9383)
>
> ….
>
> MR. NORMAN: And this goes to admissibility as well. So I'm not sure if you want us to do a motion beforehand or not.
>
> MR. JUSTICE MANSON: It's not going to go to admissibility. It's going to go to weight.
>
> MR. NORMAN: Okay.
>
> (Ebers cross, AB Vol. 32, Tab 79, p. 9385)

[53] According to the appellants, they considered this exchange to be a final ruling on the admissibility of the report. The respondents submit that the appellants in fact simply chose to abandon the point. As noted, by the time the appellants decided to raise the issue, Dr. Ebers had not only been admitted on consent as an expert but his report also had been accepted into the evidentiary record. When the matter was raised, Dr. Ebers was under cross-examination (and was about two thirds of the way through the second day of questioning) on quite a few issues and a lot of the prior art on which the appellants now rely to argue that the Federal Court did not adopt the mantle of the POSITA. That portion of their cross-examination also clearly indicates that Dr. Ebers was very knowledgeable and well informed about the literature dealing with MS and all clinical trials and studies relating thereto.

[54] During their closing arguments before the Federal Court (AB Vol. 33, at p. 9804), the appellants took the position that Dr. Ebers' report should be given little weight. I reproduce this passage because it indicates that they also appear to have made another strategic decision.

> … So we submit that the Ebers' report should be given little weight. But what does it mean?
>
> And I want to be fair to my friends. We do not take issue with paragraphs 1 to 94. That's the section Justice Manson, right before the state of the art section. We have a concern with duplication. That's not to say that we agree with it. … But we are not suggesting that 1 to 94 was improperly tainted based on what we have. … So we suggest that little weight or extreme caution should be used in reviewing the state of the art section of Dr. Ebers' report and the portion thereof. And one of the consequence of this … is that it caused Dr. Ebers' report to become a product of hindsight.

[55] This, in effect, is what the Federal Court ended up doing as it gave little weight to much of the evidence of Dr. Ebers in respect of the prior art and obviousness. But it did accept and refer to some of his evidence in respect of the common general knowledge (CGK) and claim

construction (contained in paragraphs 1-94 of his report). In such circumstances, should this Court now intervene because the appellants argue that it was an error of law not to dismiss the report on the basis that it was not impartial based on the principles set out by the Supreme Court in *White Burgess Langille Inman v. Abbott and Haliburton Co.*, 2015 SCC 23 (*White Burgess*), a Supreme Court of Canada case that the Federal Court considered and referred to in its decision in order to issue a general warning to the IP bar regarding an expert witness' duty of impartiality and independence owed to the Court? I think not.

[56] First, I do not consider the exchange referred to above as a final decision on admissibility. Asking whether one should bring a motion is not the same as asking for a ruling on one's objection. When counsel have an issue with impartiality or independence, it is incumbent upon them at that point to clearly raise an objection and present their argument. A trier of fact should not be presumed to have made a final decision on an objection when it did not even have the opportunity to review the NOA or hear submissions on the objection.

[57] Second, I am satisfied that the Federal Court was alert and alive to the principles enunciated in *White Burgess* despite the appellants' position in their closing submissions. It did note that the duplication raised an issue about this expert's report impartiality, and it is implicit from paragraphs 70-71 of its reasons that, in this case, the Federal Court did not find it appropriate to strike out the report on that basis. There is no an error of law in this finding; the Federal Court exercised its gatekeeping role as best as it could in the particular circumstances. I also have not been persuaded that it made a palpable and overriding error in not striking out the report considering the type of information that was copied in its proper context.

[58] There was no doubt that the Federal Court was satisfied that Dr. Ebers was entirely aware of all the prior art listed before referring to it in his report. The part of the report that mirrors the NOA essentially consists of citations of various passages from documents attached to his report. It would not have made a meaningful difference if he had acknowledged in his report that the passages he cited were those reproduced in the NOA because he was satisfied that they were relevant. He certainly said so during his testimony. There are paragraphs in this section of the report that were clearly added to reflect Dr. Ebers' personal knowledge, see for example paragraphs 159-165. Thus, this situation was not an egregious case or one of those rare and very clear cases where the Supreme Court has said the trier of fact should conclude that the proposed expert is unable or unwilling to meet his duty to the court and should strike his report.

[59] In C*ojocaru v British Columbia Women 's Hospital and Health Centre* 2013 SCC 30, (*Cojocaru*) the Supreme Court was faced with an even more extensive case of copying, albeit in a different context (judicial reasons). It noted that the extensive copying could create an impression that the reasons were not reflecting the judge's own thinking and thus such practice should be discouraged. But, it did not automatically follow that the judge was not impartial or independent (*Cojocaru* at paras. 35-36). I therefore conclude that one must carefully consider the exact nature of the information copied before concluding that an expert cannot perform their duty to the Court. Obviously, that is not to say that it could not have any impact on the trier of fact's overall assessment of the report of the expert and the actual weight attributed to it. It clearly did here and the Federal Court was right in issuing a warning to the bar to discourage any such practice.

[60] There is thus no reviewable error that would justify our intervention.

B. *Common General Knowledge*

[61] To facilitate the understanding of my analysis on claim construction and obviousness, it is useful to next summarize some of the CGK as found by the Federal Court (FC Decision at paras. 8-17, 86-91). CGK is relevant to both the purposive construction of the claims, as well as the analysis of obviousness.

[62] MS is a chronic progressive disease that affects the central nervous system; it is at least in part a demyelinating disease. The myelin sheath acts as an insulating substance that surrounds nerve fibers, which allows electric impulses from the brain to reach different parts of the body quickly. If this insulation, which is akin to the insulation of an electrical wire, is defective, currents in the nerve fibers lose strength (FC Decision at para. 9).

[63] A potassium channel blocker such as fampridine or 4-aminopyridine, or 4-AP (in the 277 Patent), allows for restored conduction of action potential in the demyelinated nervous fibers. Thus, fampridine has been tested as a potential treatment for MS, or more accurately as a treatment of some of its symptoms (FC Decision at para. 10).

[64] It is worth noting that the testing of fampridine as a potential treatment for MS was recognized at paragraph 76 of the 277 Patent, which states that:

> Fampridine has been shown to restore action potential conduction in damaged, poorly myelinated nerve fibers, and it may also directly enhance synaptic transmission. In previous clinical trials, treatment with fampridine has been

> associated with a variety of neurological benefits in people with MS, including faster walking and increased strength, as measured by standard neurological assessments.

[65] 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, and even for such patients, they may not be effective at all times (FC Decision at para. 17).

[66] 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 were associated with serious adverse effects. When selecting a proper dose, the POSITA would have been aware of potential adverse effects and the "start low, go slow" approach to therapy was commonly used (FC Decision at para. 91).

[67] Impaired walking or walking disability is one of the most common MS symptoms that has a detrimental effect on patients. It is one sign of the progression of the disease in terms of the practical effect MS has on a patient's daily life (FC Decision at para. 12).

[68] A difficulty with MS is that the symptoms may come and go, may persist, or often worsen over time. Given the high variability, it is very difficult to determine whether a potential treatment is having a clinically meaningful effect as opposed to whether any observed change is simply due to the inherent variability of the disease (FC Decision at para. 15), which may change on a weekly and sometimes daily basis (FC Decision at para. 89).

[69] There is also a significant placebo effect when testing MS patients for new treatments. Because of the variability in timed 25-foot walk results, for example, some researchers use a threshold of 20% improvement as a statistically significant level and as a minimum requirement when evaluating whether a given intervention (i.e. treatment) caused a particular effect, as opposed to chance improvement due to the inherent variability of these symptoms.
The significant variation in the placebo effect also makes it more difficult to detect whether the intervention provides a clinically relevant benefit (FC Decision at paras. 16, 90).

[70] Finally, in addition to approved treatments, various alternative treatments have been used in the hope that they would provide some relief from MS. Historically, certain alternative treatments have been purported to be the "next best thing" but ultimately have not passed the clinical muster. In light of these repeated "false dawns", MS researchers are highly sceptical of alternative treatment that are not supported by double-blind placebo-controlled trials
(FC Decision at para. 17).

C. *Claim Construction*

[71] Although the principles described by the Federal Court are not in dispute in this case, it is still important to reiterate that a patent's description (also referred to as the disclosure) must be considered when construing claims.

[72] As noted in *Whirlpool* at paragraph 49(e), interpreting a patent is like interpreting a regulation. Purposive claim construction involves looking at words of the claims in context. This includes in the claims individually and as a whole, considering their purpose as well as the

description. As noted by the Federal Court, the entire patent must be considered, but adherence to the claim language allows the claims to be read in a way in which the inventor is presumed to have intended, thereby promoting fairness and predictability (FC Decision at para. 78).

[73] In *Whirlpool* at paragraph 49(f), the Supreme Court reminded us that this is so because the point of the analysis is to interpret and respect the inventors' objective intention as manifested in the words he used. This is why the whole disclosure must be reviewed, even for words that would appear at first glance to be simple and unambiguous when reading only the claims. Indeed, one of the reasons for reviewing the disclosure is to determine whether the inventor actually defines particular words that could appear plain and simple even to a POSITA when reading only the claims (*Whirlpool* at para. 52 & 54, definitional assistance). Obviously, and as is well-known by those in the field of intellectual property law, the technical terms or so-called terms of the art must be read through the lens of the POSITA. However, as also noted by the Supreme Court in *Whirlpool* at paragraph 61, a Court is entitled to differ from the construction put forth by either side for it is its task to construe the claims as a matter of law. This is because the role of the expert is not to interpret the patent claims *per se*, "but to put the trial judge in the position of being able to do so in a knowledgeable way" (*Whirlpool* at para 57).

[74] The main purpose of claim construction is to identify the essential elements of the subject matter as claimed. In that respect, once again, the inventor's objective intention is what a Court is trying to ascertain. In this case, the parties had agreed on what should be considered essential elements of the asserted claims but they had not completely agreed, for reasons explained later,

on what each such element encompassed or meant. Still, the Federal Court had to perform its own analysis to confirm these elements. It clearly did so.

[75] As mentioned, before us, the appellants only challenge the construction of the words "use for improving walking" and "use for increasing walking speed". They argue that the words "improving" and "increasing" would be understood as directed only to "clinically meaningful" improvement or increase and therefore require two essential elements: a meaningful quantitatively measured improvement or increase that is also subjectively assessed as meaningful by the "subject with MS in need thereof".

[76] The Federal Court construed these words as referring only to a meaningful quantitative improvement or increase, i.e. one that would be statistically significant so as to take into account the variability of symptoms and the prevalence of placebo effect in MS patients (see paras. 16, 20-21 above).

[77] Although, the appellants focussed their argument on what they consider conclusive evidence of agreement between the experts as to how the POSITA would construe these expressions, I cannot limit myself to examining this evidence. In this case, the Federal Court found that the construction put forth by the appellants was contrary to a purposive construction of the claims. I will thus proceed with my analysis using the CGK as articulated by the Federal Court before reviewing the evidence relied upon by the appellants.

(1) The Language of the Claims

[78] At paragraph 6 of my reasons, I mention which of the 112 claims of the 277 Patent were at issue in this litigation. All relevant claims are reproduced in Appendix A to the FC Decision.

[79] For my purposes, I only need to reproduce the following three claims, which sufficiently encompass the language on which I must focus on this appeal.

Claim No.	Claim Language
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.
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.

[80] I do not intend to discuss the essential elements identified by the Federal Court such as "subject with MS in need thereof" or of additional elements in other dependent claims such as "C_{avSS}" or "T_{max}". These are not in dispute. Subject to my comments in paragraphs 97-98 below, I generally agree with the Federal Court's findings (see paras. 16, 20-21 above). As mentioned, it is clear from the construction adopted by the Federal Court in respect of these elements that it

considered the expert evidence as to their technical meaning (see for example para. 18 above). It also considered the CGK (see for example the FC Decision at paras. 13, 87 and para. 16 above).

[81] The main difference between all of the independent claims in the 277 Patent is that each refers to a specific purpose for the use of the 10 mg dose of fampridine SR twice daily:

(i) In claims 1 to 14, the said dosage of this drug is used for treating MS;

(ii) Claims 15 to 28 are directed to its use for improving walking;

(iii) Claims 29 to 56 apply to its use for increasing walking speed;

(iv) Claims 57 to 70 apply to its use for improving lower extremity muscular tone (LEMT);

(v) Claims 71 to 84 are directed to its use for improving lower extremity muscle strength (LEMS);

(vi) Claims 85 to 98 apply to its use for improving quality of life; and finally

(vii) Claims 99 to 112 apply to its use for reducing spasticity.

[82] None of the claims includes any other words that characterize or quantify the expression "use for improving", "use for increasing" or "use for reducing". On their face, these commonly used words would appear plain and simple. Dr. Oh also confirmed that they were plain and unambiguous in her view (AB Vol. 32 at p. 9153-9154). Before considering Dr. Leist's and Dr. Ebers' evidence I will review the disclosure, for as mentioned this is where the inventor may give an indication of his objective intention which may impact the interpretation suggested by the experts.

[83] At this stage, the purpose of the claims appears clear. They related to the use of 10 mg bid (i.e. twice daily) fampridine SR as a treatment. The Swiss-type claims like claim 18 have been regarded as simply another way of claiming such use but against the manufacturer of the medicament. In that sense, those claims are addressed to their activities but there is no evidence that they should otherwise be construed any differently.

[84] Considering the CGK described by the Federal Court to be a treatment, i.e. the result of the administration of the active ingredient, "use for improving" for example, would at least be understood by the POSITA as directed to an improvement over and above the known variability of the symptoms in MS patients, as well as those linked to the placebo effect that may have an impact when MS patients are given any treatment.

[85] The appellants do not disagree with this.

(2) The Description

[86] I have decided to go into more detail in these reasons than what one would normally expect from an appellate court to illustrate how construing a patent is more than reading the claims and adopting whatever construction the experts put forward on the sole basis that this is how a POSITA would construe them.

[87] I will start by reiterating that the disclosure in this patent describes much more than what is claimed, not only in terms of the diseases for which a composition of 10 mg bid fampridine SR can be used (277 Patent paras. 0003, 0005, 0010 for example), but also the therapeutically

effective dosage (see 277 Patent paras. 0010-0015, 0046-0047), and the frequency of administration of the fampridine SR dosage (see 277 Patent paras. 0014, 0015, 0053). And, most importantly, the patent deals at length with embodiments and particular methods for selecting responders (see 277 Patent at paras. 0019-0020,0027-0028,0030,0032,0077-0084 and a large portion of Example 5) that are no longer claimed.

[88] While the description covers a lot of information that is not relevant to the subject matters claimed, I found no example or discussions where the effect of the active ingredient is directly related to the use of the claimed dosage after only two weeks of administration. The experts did not refer to any such passage that could explain the choice of two weeks as a minimum duration in some of the claims. Example 5 in the description is the only one dealing with efficacy. It describes a 20-week clinical trial, where the stable treatment phase lasted 12 weeks for the 15 mg and 20 mg bid dosages (although the 10 mg bid was used for 14 weeks, as there was titration for this dosage). There were visits every two weeks after the start of the stable treatment period, plus five visits when no treatment was administered (four visits before and one after the stable treatment period) (277 Patent at paras. 00101-00102).

[89] All the information and data included in Example 5 with respect to the so-called *post ho*c responder analysis do not appear to be helpful without some explanation from the experts. The responders group included four placebo subjects and 58 fampridine-treated subjects overall for all the three dosages tested (10 mg bid, 15 mg bid and 20 mg bid). I note that of this group, only 18 subjects were treated with the claimed dosage (10 mg SR bid), and all these responders were chosen based on their response during at least three visits while on stable treatment. Thus, I

understand that all the efficacy results disclosed cover a period of at least six weeks of stable treatment. It is certainly not clear to me that for any or all the so-called responders, such visits necessarily included their first one after the first two weeks in the stable treatment phase.

[90] There is no expert evidence confirming that an inference as to the minimum time period of two weeks can be made from this data. In fact, Dr. Ebers testified that it was not clear to him on what basis that minimum period of two weeks was chosen. Dr. Leist simply avoided the issue by construing the claims that referred to "at least two weeks" as meaning that it is the improvement that must be consistent for at least two weeks, rather than the use of the dosage for at least two weeks (see para. 83 of his report). I note that Dr. Leist appears to have misunderstood Dr. Ebers' construction in that respect (see Dr. Ebers' report at paragraph 87 where he construes the claims as requiring that the 10 mg fampridine -SR composition be administered for at least two weeks, and Dr. Leist's report at para. 446). But more importantly, this evidence was expressly rejected by the Federal Court. I understand that the Federal Court considered it as part of "the tortured construction" offered by this expert witness, trying to incorporate Example 5 (here the criterion of consistency used in the responder analysis) into the subject matter claimed (see FC Decision at para. 104). I can certainly agree with this finding of the Federal Court. It is simply not what the claims say, and there is no valid reason for a POSITA to construe the clear wording of the relevant claims otherwise.

[91] This, in my view, offers a good illustration of how a court may reject expert evidence as to how a POSITA would read a claim when it is simply not supported by a proper application of the purposive analysis to claims construction.

[92] Turning back to the description, the section entitled “Background” starts by stating that the invention relates to a dosage form of a fampridine SR composition that maximizes the therapeutic effect, while minimizing adverse side effects (see 277 Patent at par.0002). It offers limited information, but it does generally confirm what was commonly known about the mechanism of potassium blockers such as fampridine in the symptomatic treatment of spinal cord injury, MS and Alzheimer’s disease (see 277 Patent para. 0005).

[93] In the section entitled “Summary of the invention”, the inventors describe various embodiments where they first use the words “for increasing” and “for improving” without any qualification. I note that the most often used expressions in this section is “therapeutically effective” or “effective amount” of the active ingredient or of other key components of the composition. It is also clear that the various embodiments up to paragraph 0019 are to provide a treatment of symptoms related to the degradation of nerve impulse transmission. It is only in paragraphs 0019 and 0020 describing the embodiment of methods of selecting individuals, based on responsiveness to a treatment (a subject matter not claimed), that the inventors first refer to the administration of various tests to identify individuals exhibiting “an improved performance” during a majority of the tests administered during the treatment period.

[94] In the section entitled “Detailed description of the invention”, the inventors start by stating that the invention is not limited to the methodologies or protocols described in the disclosure and may vary. The terminology is only used to describe particular versions or embodiments (277 Patent para. 0033). This is an often-used clause as this is not always well understood by those unfamiliar with reviewing patents, including technical experts.

[95] I ought to mention here that it is not disputed that except for the *post hoc* responder analysis, which is the subject of debate, all the methods or tests used, either to make the compositions of fampridine SR or to determine the safety and efficacy of the dosage claimed were well-known (see for example 277 Patent para. 0058).

[96] This section also indicates that "[u]nless defined otherwise, all technical and scientific terms used therein have the same meanings as commonly understood by one of ordinary skill in the art" (277 Patent at para. 0035). There are many such technical terms throughout the disclosure. But this does not mean that every word used is a technical or scientific word. The inventors then proceed to give specific definitions of certain expressions used in the patent, which may well differ from what would be commonly understood by the POSITA. Obviously, these definitions are quite important, because an expert must provide a persuasive explanation as to why a particular definition should not be adopted by the Court. None of the experts referred to the following definitions in their reports.

[97] First, the terms "patient" and "subject", which are used in all the asserted claims, is defined to include all animals, including humans (277 Patent at para. 0037). It is clear from paragraph 007 that animals can naturally suffer from spinal cord injuries or diseases. It may well be that this definition could not have been appropriate if the subject matter claimed is MS only, because such disease only affects humans. Still, I find it somewhat surprising that no explanation was given, especially by Dr. Leist who insists that a subjective assessment by the subject in need of treatment is an essential element of the subject matter claimed. Obviously, if other primates are included, one could hardly require a subjective assessment. I note that the fact that the

inventors tested humans only in the Examples sections would not likely be a proper explanation to disregard an express definition. Examples do not define the parameters of the claims.

[98] That said, for the purpose of this appeal, I am prepared to assume that MS is a purely human disease, which is essential to the appellant's argument. This was not disputed by the respondents.

[99] The definition of "therapeutically effective amount" is also of interest (277 Patent para.0041), given that the claims all include the particular dosage to be used. It is defined as "an amount sufficient to decrease or prevent the symptoms associated with a medical condition … or to provide improvement in one or more of the clinically measured parameters of the disease".

[100] The next term of interest is "treatment" (277 Patent para. 0042). It is a long definition. I will only refer to the portions which offer some indication in respect of the issue before me. It refers to "the administration of the medicine for … amelioration [of] the clinical condition of the patient … or subjective improvement in the quality of life of the patient". This definition would appear to support the respondents' position before us that a subjective assessment of the improvement was only objectively intended by the inventors in respect of claims 85 to 98, which relate to the use of 10 mg bid of fampridine SR for improving quality of life . Quality of life is not a symptom of MS *per se* but rather the overall impact of these symptoms of MS on the patient. *A contrario*, the reference to clinical condition of the patient appears in line with the above quoted passage which refers to improvements in "clinically measured parameters of the disease".

[101] None of the other definitions includes information that may be relevant to my analysis. There is no distinct definition of the word “improvement” *per se*, or of the phrase “use for improving or for increasing”.

[102] At paragraph 0044, the inventors note again that a therapeutically effective amount of fampridine SR is the amount that, when administered to a patient or subject, ameliorates a symptom of a neurological disease. Ameliorates is a synonym of improving that does not appear to be intended to convey a particular scientific meaning other than what as already been noted.

[103] Given the importance the appellants’ accord to Example 5 in the 277 Patent and the *post hoc* analysis, it is worth noting that at paragraph 0078, the inventors specify that even in respect of the method of selecting individuals based on responsiveness to treatment, “this embodiment selects subjects who show a pattern of change that is consistent with a treatment response, but does not define the full characteristics of the response”. The “criterion itself”, that is consistency over a certain number of visits during the stable treatment period, “does not specify the amount of improvement nor does it specify that the improvement must be stable over time”.
The inventors simply state that the *post hoc* analysis discussed in Example 5 indicates that one “may expect responders defined by a consistency of effect to also demonstrate increased magnitude and stability of benefit”.

[104] The rest of this section deals with why the clinical trial as originally designed did not establish a statistically significant difference between the placebo and the fampridine SR treated subjects, even though a large proportion of such subjects did show an improvement. These

paragraphs may be relevant to the obviousness analysis (by providing some objective evidence as to the thinking and conduct of the inventor) but they bring little to construction of the claims. I note, however, that in the last sentence of paragraph 0079, after stating that it is not possible to pre-select potentially responsive patients prior to a trial because of the insufficient understanding of the disease, the inventors state that "the existence of the subset of patients who respond consistently to the drug can be supported by quantitative observations in our clinical studies discussed below".

[105] Then, at paragraph 0084, the inventors indicate that all dosages tested were found to be effective in the responder group, showing a highly significant and consistent difference between placebo and drug treatment groups. This was confirmed by the pooled fampridine SR treated groups against the placebo treated group (58 subjects versus four). Both experts appear to agree in their reports that in their reading of the description, the ultimate choice of 10 mg bid dosage was based on the favorable adverse effect vs efficacy profile.

[106] In discussing the magnitude of the change, the inventors refer to the statistical information of >25% average increase in walking speed over the treatment period. It is also in that paragraph that for the first time, the inventors indicate that the responder group, also showed an increase in Subject Global Impression score, and an improvement in the score on the MSWS-12.

[107] The words "clinically meaningful" are not used in the "Detailed description of the invention" section of the 277 Patent. The first time a similar expression is used is in the context

of Example 3 dealing with the pharmacokinetic properties of the fampridine SR tablets, which also deal with the safety evaluation of the proposed drug. At paragraph 0093, the inventors state, after describing some adverse events, that "there were no clinically significant change in the clinical laboratory values, ECG parameters, vital signs, physical examination findings, or neurological examination findings noted over the course of this study".

[108] The same expression is again used at paragraph 0099, under Example 4, where one finds a sentence stating that "there were no clinically significant change in the mean clinical laboratory values, vital signs, or physical examination finding from baseline to last visit". The trials described in Examples 3 and 4 were open label with 23 subjects and 20 subjects respectively.

[109] This brings me to Example 5, which is said to exemplify an embodiment of a method of treating subjects with fampridine and an embodiment of the responder analysis of the present invention (see first sentence of para. 00101). It is only an embodiment of the method of treating subjects in need thereof in the sense that it describes the dosages actually used, how often they were taken, and for how long. As mentioned, one must be alert and alive to the fact that the responder analysis is no longer an embodiment of a subject matter claimed. This Example simply informs on the relevance of the reorganized data after the *post hoc* analysis to establish or soundly predict that the claimed dosage can indeed treat the symptoms described in the claims in certain MS patients called the responders. It also informs that the consistency of quantitatively measured improvements may be a suitable outcome measure in future clinical trials.

[110] The sufficiency of the information given or its persuasive impact as to the ultimate efficacy of the subject matter claimed, based on the *post hoc* analysis performed, or the utility in respect of the various symptoms covered in the claims, was not in issue even if both side experts offered various comments in that respect. It is not relevant to the present analysis. But one can safely assume that this was an important aspect for the inventors if this Phase II clinical trial (see 277 Patent para. 00101) was to be found sufficient to enable them to ultimately proceed further on the basis of similar responder analysis and get the FDA approval of a medicament (277 Patent at para. 00131).

[111] There is no need to insist on the repetitive reference to statistical data in this section. This is quite understandable, given that many of the endpoints, not only the primary one, were quantitative tests relating to various symptoms experienced by MS patients. What is of interest is how the expression "clinical meaningfulness" was used in Example 5 of the 277 Patent.

[112] The first time the term "clinical meaningfulness" appears in the 277 Patent is at paragraph 00106, where after being satisfied that the *post hoc* responders analysis based on a subject by subject analysis of the consistency of quantitative (i.e. statistical) response over at least three visits, inventors state "to validate the clinical meaningfulness of the *post hoc* responder variable, the (*post hoc*) responders were compared against the (*post hoc*) non-responders, on the subjective variables". Once again, the *post hoc* responder variable in question here is the consistency of the quantitative improvement as a result of treatment, as opposed to simply quantitative results. The same statement is repeated again in the first sentence of paragraph 00123. Interestingly, the inventors specify that consistency in walking speed had

"clinical meaningfulness for the subjects in this study" and conclude with a somewhat puzzling last sentence if one's objective intention is to make clinical meaningfulness based on subjective variables an essential element of the claims: "thus, responders experienced clinically meaningful improvements in their MS symptoms and treatment with fampridine significantly increased the chances of such a response" [emphasis added].

[113] Before repeating the statement about the validation of the criterion at paragraph 00106, as I noted in my reasons above at paragraph 112, the inventors state, at paragraph 00120, "subsequent analysis revealed the existence of a subset of subjects who responded to the drug with clinical meaningfulness. These subjects exhibited walking speed while on drug that were consistently better than the fastest walking speeds measured when the subjects were not taking active drug". Here the last sentence appears to link clinical meaningfulness to exhibiting consistently better walking speeds that were quantitatively measured.

[114] At paragraph 00125, the inventors again specify that having demonstrated the clinical meaningfulness of consistently improved walking as a criterion for responsiveness, the question of magnitude of the benefit becomes of interest. They calculated it on a statistical basis and conclude that it is highly significant, given that it ranged from 24.6% to 29%, compared to 1.7% to 3.7% for the placebo group (277 Patent para. 00126). They then note this improvement was stable and was "associated" with improvement on two of the five subjective tests described in paragraph 00101.

[115] At paragraph 00127, the inventors also note that their results also suggest that "although a clinical meaningful response can be linked to about 37% of the subjects treated with Fampridine-SR [the *post hoc* responders], additional subjects may have functional improvements on variables other than walking speed" [emphasis added].

[116] Finally, at paragraph 00131, after stating that their responder analysis provides a meaningful approach and may be used as a primary endpoint in future trials, the inventors state that their data suggest "that for the responsive subjects (approximately 37%) treatment with fampridine at doses10-20 mg bid produces substantial and persistent improvement in walking".

(3) Expert Evidence

[117] As mentioned earlier, the appellants say that the experts agreed that a POSITA would read in the words "for improving" or "for increasing"; the words "in a clinically meaningful way", and that these words necessarily include in this essential element of the claim a subjective assessment by the individual subject. But it is not disputed that such an assessment could only be made after the subject has received the treatment over at least two weeks through the use of tests such as the MSWS-12 referred to in Example 5 of the 277 Patent (no sample of such test is in the evidentiary record before us).

[118] I underline here that this is not a case where the words "clinically meaningful" are used in any of the claims, in which event, the issue would be how a POSITA would construe these words.

[119] With respect to "for improving walking" , Dr. Ebers, in his report at paragraph 84, states that given the variabilities, the POSITA "consistent with their common general knowledge and the repeated reference to statistical significance in the 277 Patent would understand 'improving walking in a subject' … in claim 15 to refer to a statistically significant increase in walking, rather than just any anecdotal observed increase that might be unrelated to any active ingredient" (see also para. 30 of his report responding to Dr Oh's report). This is consistent with the Federal Court's finding. At paragraph 441 of his report, Dr. Leist clearly states that this statement of Dr. Ebers appears to be consistent with his understanding that Claim 15 relates to a clinically meaningful improvement in walking. He says, "I believe we are saying the same thing in different words".

[120] At paragraph 86 of his report, Dr. Leist adds that "a skilled person would only consider walking to be improved … if a quantitative improvement is also clinically meaningful. In other words, a faster T25FW [25-foot timed walk] (*e.g.* 12 seconds vs 12.1 seconds) that did not have any perceived benefit to the patient would not be understood by a Skilled Person to constitute an improvement in walking in an MS patient with walking disability".

[121] Despite this, at paragraph 236 of his report, while examining prior art, Dr. Leist says that the author did "not report the magnitude of the improvement, such that the Skilled Person could try to surmise, whether the reported statistically significant improvement was clinically meaningful" [emphasis added]. Does this mean that in this case "clinically meaningful" only refers to the magnitude of the improvement or does this mean that the POSITA does not

necessarily need a patient's suggestive assessment of an improvement to determine that it is clinically meaningful?

[122] During his cross-examination, Dr. Ebers was asked about an article he wrote about guidelines for clinical trials where he had written that the outcomes should be realistic and clinically important. He used the following example to illustrate what he meant by referring to many papers in the MS context dealing with better MRI scan, noting that the patients "don't care a whit if their MRI scan is lovely". He then simply agreed with the suggestion of counsel that an outcome must be clinically meaningful (AB Vol. 32 at p. 9289). It is worth mentioning here that the Federal Court found that as a matter of CGK, that walking impairment has detrimental effects on MS patients, and has a practical effect on their daily life.

[123] The appellants have made much of the last portion of paragraph 91 of Dr. Ebers' report (dealing with claims 30-42), which is in the section of his report in respect of which they did not raise any objection in their closing argument before the Federal Court, making what appears to be a strategic decision to preserve their ability to rely on this paragraph. There, Dr. Ebers says that "any increase in walking speed would be considered an improvement in walking" and "the skilled person would also understand that an isolated increase in walking speed would have to be clinically meaningful, with perceived benefit, not just a statistical finding among responders".

[124] Dr. Leist noted in his report that there must be a typo or something wrong in the first sentence of this passage, for he could not understand how any increase in walking speed could be an improvement. But the appellants did not try to clarify this passage; they did not raise

paragraph 91 at all with Dr. Ebers in their cross-examination. I find this whole passage in paragraph 91 to be ambiguous in light of paragraphs 84 and 30 of his reports At paragraph 84, Dr. Ebers'says the skilled person "would understand 'improving walking in a subject…' in claim 15 to refer a statistically significant increase in walking, rather than just any anecdotal observed increase that might be unrelated to any active ingredient". Does he use isolated to mean the same thing as anecdotal? If "clinically meaningful" is, as suggested by Dr. Leist, a technical term commonly understood as including a subjective element, there would be no need to add "with perceived benefit". This extract is not as conclusive as the appellants purport it to be and weighing evidence is the role of the trier of fact.

[125] Triers of fact benefit from a presumption that they have considered the whole record before them. This presumption is especially difficult to rebut here, when the appellants specifically read, during their closing submissions, paragraph 91 of Dr. Ebers' report, as well as the above mentioned answers in cross-examination (as discussed in paragraph 121 of these reasons above and see AB Vol. 33 p. 9806-9807). They made the same argument before the Federal Court that they made before us. There is no doubt in my mind that the Federal Court considered this evidence, despite the fact that it did not expressly referred to it in its reasons. So is this evidence sufficient for this Court to conclude that the trier of fact erred by not adopting this proposed interpretation of the claims, i.e. that it necessarily includes perceived benefits as assessed by the patients?

[126] As mentioned, I understand from paragraph 95 of the FC Decision that the Federal Court refused to construe the claims as meaning that an improvement needs to be clinically meaningful

because on a purposive construction, the subjective element, which was included in this notion certainly by Dr. Leist, does not form part of the claimed invention.

[127] The Federal Court did not disagree that in clinical practice, the continued use of the fampridine treatment may well depend in part on the patient's perception of the resulting improvement. Most laypersons of my generation would know that often, the first questions from your doctor after you have started a new treatment that can have adverse effects, and is not always 100% effective are something like "How are you doing? Does it help?"

[128] What the Federal Court said was that it was simply not appropriate to read into the claims as written a subjective assessment of the efficacy of the treatment. I understand this to mean that this would simply not be fairly representing the objective intention of the inventors. I agree with this for a number of reasons.

[129] First, it is absolutely clear from a proper reading of the description that the inventors did not intend to claim any particular result other than that this fampridine SR composition may be used as a treatment; i.e. that the administration of the claimed dosage as described in the claims can have an impact in some patient in need thereof that are attributable to the active ingredient.

[130] The inventors did not make any promise that any patient who is responsive to the active ingredient will indeed have an improvement that they subjectively perceive as a beneficial or a sufficient improvement to justify taking the medicament. I use the world "promise" here in a

generic way not intending to refer to the promise doctrine that was rejected by the Supreme Court but which appears to have had some influence on Dr. Leist's understanding of the claims.

[131] Second, the inventors were familiar with the words "clinically meaningful" and they did use them when they meant to validate the criterion they used in their *post hoc* responder analysis and the improvement of the actual responders in Example 5. They never used them in the "Detailed description of the invention". They also made it clear the invention was not limited to any methodology issued in the examples (see para. 94 above).

[132] From the evidence referred to above, the meaning of these words appears to change depending on its context and this is the case even for the experts themselves. Dr. Ebers agreed that clinical studies should provide clinically important or meaningful outcomes, but this is irrelevant to whether one cannot seek a patent for a treatment that may not be widely used because the POSITA is not persuaded of its importance or meaningfulness. Under patent law, the treatment only need to be useful.

[133] I note that no technical dictionary definition or literature was provided to the Federal Court to confirm that indeed, the expression "clinically meaningful" always includes a subjective assessment by the patient. In Example 5, the clinical trial used as one of its subjective variables tests the Clinician Global Impressions (CGI), which only rated the actual responders marginally better than the non-responders during the double blind (277 Patent at para. 00123). Is there more than one subjective point of view that is relevant to clinical meaningfulness? It is dangerous to add words into a claim when their meaning itself is ambiguous.

[134] In defining the parameters of the CGK, the Federal Court used the words "clinically meaningful" but only in the context of determining whether a potential treatment was having an effect as a treatment, i.e. as the result of an active ingredient as opposed to the known inherent variability of the symptoms (see para. 68 above). I do not view this as being in contradiction with its finding that the words "clinically meaningful" as professed by Dr. Leist should not be read into the claim. It is clear that the Federal Court did not use or understand them as including a subjective component.

[135] It may well be that it would have been advisable to use the word such as "clinically significant", given the debate on the meaning of "clinically meaningful". Still, as mentioned, the Federal Court is not to be held to a standard of perfection (*Millennium Pharmaceuticals Inc. v Teva Canada Limited,* 2019 FCA 273 at paras 8-12), and it made it clear in what sense it used these words. The findings at paragraphs 15 and 16 of the FC Decision were not disputed at all before us.

[136] Turning back to the inventors' objective intention, not only did they not use the words "clinically meaningful" in any claim, but they also did not to use words like "consistently" in the claims, even if this was their main criterion in the responder analysis to describe the quantitative improvement measured in the responders in Example 5.

[137] Like many other choices they made, such as limiting the claims to treatment of MS only, or to the 10 mg bid dosage, they chose to claim the use for improving various symptoms in <u>all</u> MS subjects in need thereof.

[138] They could have claimed such use only in responders, i.e. patients who consistently exhibited a statistically significant improvement that was “associated” with a perceived benefit by the responders in their clinical trial. They did not.

[139] Accepting the interpretation proposed to us by the appellants would totally change the monopoly as claimed. It would only apply after an individual subject has been identified through the actual use described in the claims as a responder using the method set out in Example 5 or a derivative thereof. This interpretation appears again to have been influenced by Dr Leist’s tortured construction aimed at incorporating the *post hoc* analysis into the claims which the Federal Court referred to more than once and rejected. I agree.

[140] The Federal Court construed the claims by reviewing the patent as a whole in light of the CGK (i.e. reading it through the eyes of a POSITA). In my view, the Federal Court did not err by failing to adopt as argued the mantle of the POSITA.

[141] On my reading of the reasons of the Federal Court, it also did not err as suggested by the appellants by failing to include a specific percentage to measure what effect is above the inherent variability of the symptoms and placebo effect. As found by the Federal Court, the 20% threshold in walking speed used by the inventors in Example 5 is only one measure commonly known to be use in some clinical trials. There may be others and such measurement techniques may evolve.

[142] I have also not been persuaded that the Federal Court made a palpable and overriding error in assessing the evidence referred to above and that it was not useful to reach its conclusion on the meaning of the claims. There is no basis for this Court to intervene.

D. *Obviousness*

[143] Pursuant to section 28.3 of the *Patent Act*, R.S.C., 1985, c. P-4, the subject matter of a claim must not be obvious. This is the only real guiding principle. All the tests and criteria developed by the Court, including the Supreme Court of Canada in *Sanofi*, are meant to be aids to the Court to reach a conclusion in that respect. These are to be applied with flexibility and the importance given to any factor depends on the particular facts of a case. Determination of whether an invention is obvious to a POSITA is based on a multifactorial balancing. This means that courts of appeal must be particularly attentive in their application of the standard of review. This is also why one must be cautious before finding an extricable error of law that would bypass the stringent standard applicable to such factual conclusions.

[144] The Federal Court enunciated the principles and the factors it considered for its claim-by-claim analysis. They are not in dispute. I will thus start with the first main issue raised by the appellants: whether the Federal Court made an extricable error of law by actually failing to adopt the mantle of the POSITA.

[145] I understand that the appellants rely mainly in this respect on the fact that the Federal Court essentially discarded all of their expert's opinion and their cross-examination of Dr. Ebers. This appears to be their own assessment of the Court's treatment of the evidence, for this is not

what the Federal Court said in its decision. In any event, they say that as a result of this, the Federal Court did not take into account the skepticism regarding alternative MS therapies that it acknowledged was part of the CGK (see paragraph 70 above) to assess the prior art and its impact on the ability of the POSITA to "bridge the gap" between the inventive concept and the state of the art.

[146] This argument is essentially a factual one and invites this Court to re-weigh the evidence, which is not our role. For the reasons that follow, I conclude that the Federal Court did not make a reviewable error in its assessment of the evidence and that there was sufficient evidence before it to support its obviousness finding.

[147] I commence by noting that the Federal Court expressly acknowledged that little weight was to be given to "much of the expert opinion evidence on obviousness, particularly as to how the POSITA would interpret and understand the prior art made its task difficult" (FC Decision at para. 169). That statement indicates that the trier of fact was alert and alive to the difficulty raised by its assessment of the expert evidence. It is implicit that it still felt confident that it had enough remaining evidence to perform its task in accordance with the principles and factors applicable to the obviousness analysis that it set out in its reasons.

[148] The Federal Court also expressly addressed the issue raised before us (FC Decision at paras. 130, 170). It was aware of its finding that a POSITA, especially one involved for a very long time in the field, would be skeptical of new alternative treatments that are not supported by double-blind, placebo-controlled trials. But it did not accept that this meant the POSITA would

not understand what the prior art clearly stated when read with a mind willing to understand, and would learn nothing from it unless it was absolutely persuaded of the validity of the statements made and had all the details of the study or trial reported in the prior art before being so persuaded. This finding was one that was open to the Federal Court to have made.

[149] It is also worth mentioning that the skepticism acknowledged by the Federal Court because of the so-called "false dawns" came as explained during Dr Ebers' cross-examination from a monograph called *Therapeutic Claims in MS* written years ago and dealing with the history of MS from the 1900s to 1990s when the placebo effect of potential treatments in MS patients was not duly considered. It was acknowledged by Dr. Ebers that this concern was largely addressed by the use of placebo-controlled groups in clinical trials.

[150] Most scientists are cautious, and in many fields, they would describe themselves as skeptics, but this does not mean that in all those fields the standard for obviousness becomes certainty, and most especially not in a pharmaceutical field where the "obvious to try test" was sanctioned by the Supreme Court in *Sanofi*. In fact, if the POSITA here did not believe anything they read unless it had all the details described in Dr. Leist's evidence and the benefit of large trials (which appear to have been relatively rare with MS patients given that there were few approved drugs for this disease), one wonders why anybody bothered publishing and reading all the prior art referred to by both experts, and why as many as 10,000 people gather at the conferences where abstracts and presentations like the ones before the Federal Court are made public.

[151] There is a difference between the kind of skepticism that was not accepted by the trier of fact and the type of prejudices referred to in the case law put forth by the appellants. It is one thing to say the POSITA commonly believed that a certain ingredient or test was necessary while in fact it was not. For example, Dr. Leist's evidence regarding the Schwid publication and the alleged general belief arising therefrom that a serum 4-AP levels above 60 ng/mL was required for efficacy even if based on six out of nine patients (hardly the type of study that Dr. Leist described as persuasive when discussing other prior art) and qualified by the word "appears". It is another to say that nobody would believe any result reported, however respected and cautious the author might be, or would do anything with the information unless they were satisfied that what is written is the "final word", an expression used by Dr. Leist on cross-examination, or that the evidence is so convincing that the conclusion is inescapable. The Federal Court was faced with both types of issues and addressed them quite differently, as it was open to it to do (see FC Decision at paras. 159-161 and 188-189 for the Schwid reference).

[152] The Federal Court made it clear that it adopted the perspective of how a motivated POSITA would understand the prior art with a mind willing to understand as is said in *Sanofi* at paragraph 25 (dealing with anticipation but, this approach applies equally to the obviousness analysis). This expression means that the mythical POSITA is meant to read the prior art with a view to trying to discern the intent of its author when one uses the same meaning of the expression as was said in *Whirlpool* when dealing with purposive construction.

[153] At paragraph 171 of the FC Decision, the trier of fact summarized his findings in relation to the state of the prior art at the relevant date. The first sentence of this paragraph clearly

indicates that the Federal Court focused on the relevant information that a POSITA who is willing to understand would learn from the prior art. The Federal Court explained in other parts of its reasons why other information also contained in the prior art was no longer relevant. It also explained why for example, the failure of the ten-year-old Elan trial in the Schwid reference was not teaching away from the claimed invention as suggested by the appellants (FC Decision at para. 188).

[154] I am mindful that the appellants also challenge the finding that a POSITA would be motivated because of their "skepticism". But I am satisfied that there is no reviewable error in that respect either because it was open to the trier of fact to find that such motivation existed. In addition to what is expressly mentioned in the Federal Court's reasons, there was other evidence on the record to support such a conclusion.

[155] Here, the reasons of the Federal Court are not as exhaustive as one may have hoped, but in my view, the Federal Court was not required to deal with each and every piece of prior art discussed by the experts. The Federal Court did sufficiently engage with all the major issues that were raised and argued before it by the appellants. The Federal Court made distinct findings in respect of each of them. Before us, most of these issues were reargued again based on evidence that the trier of fact is presumed to have considered.

[156] It is also important to mention that when one carefully considers the evidence in chief of Dr. Leist, it becomes apparent that the concerns expressed by the trier of fact about his persistent inclusion of the detailed responders analysis into his reasoning on obviousness (FC Decision at

para. 195) and his constant reference to clinical meaningfulness (which includes in his view a subjective component) in this section of his report (such as at paras. 356, 357, 360, 374, 375, 386, 397, 399 of his report) had a major impact on the weight attributed to his evidence on obviousness as a whole. I see no reviewable error in this regard.

[157] In addition, there is no dispute that both parties and their experts agreed that, as found by the trier of fact, the POSITA would primarily look to more recent publications to understand the state of the art rather than earlier studies that may have been superseded (FC Decision at paras. 155, 186). This explains why the Federal Court put more weight on the most recent prior art relevant to identifying an effective therapeutic dosage for fampridine SR, which is an active ingredient whose mechanism of action was understood to be useful in some (not all) patients with certain symptoms associated with the demyelination of nerve fibers. Accordingly, it focused on prior art references such as Hayes reported in 2003 in *Clinical Neuropharmacology*, Vol. 26, No 4, pp 185-192 (AB, Vol. 12, at p. 3412) (dealing with fampridine SR as opposed to another 2003 Hayes study of compounded or immediate release fampridine on which the appellants focused) and the so-called Goodman references.

[158] I am satisfied that the Federal Court also had evidence as to how a POSITA would understand the words used by these authors and what portions of these references they would consider helpful to determine the intent of its authors.

[159] When read in context including the evidentiary record, I understand that the Federal Court was careful in what information it gathered from the Goodman references. This clearly

included information obtained during the cross-examination of Dr. Ebers. It correctly understood, as both experts had agreed, that the Goodman references only reported some of the results of the MS-F201 double-blind placebo-controlled trial of 36 subjects that was carried out by a team led by Dr. Goodman which included Dr. Cohen. It did consider that such report did not include detailed results about the efficacy of the fixed dose of 10 mg bid or any other dosages actually administered (a wide range was tested from 10 mg to 80 mg per day); rather, it included the results of pooled data obtained for a range of dosage 10 mg bid to 25 mg bid (similar to what was done during the MS-F202 trial described in Example 5 for the range of 10 mg bid to 20 mg bid) (see para. 105 above). It correctly noted that the 10 mg bid dosage of fampridine SR was not administered for a period of at least two weeks. It considered the safety data contained therein, which was the primary purpose of this trial, and clearly reported that dosages of fampridine SR up to 20 mg bid had the best safety profile because dosage at 50 mg per day (25 mg bid) or higher had caused more severe adverse effects, including two seizures at 60mg and 70 mg per day (30mg-35mg bid).

[160] It was both not disputed by the experts, and is undisputable, that adverse effects and safety profile are key to determining what dosage one would even consider suitable as a treatment in MS patients. Considering that the POSITA, based on their CGK would “start low and go slow”, it was open to the Federal Court on the basis of the safety profile disclosed in Goodman (confirmed by Hayes 2003 as will be further discussed below) to conclude that it would be understood by the POSITA based on the latest art that any future study should concentrate on dosages lower than 50 mg per day.

[161] With respect to efficacy, which was the secondary purpose of the MS-F201 trial, the authors reported that "the fampridine SR group showed statistically significant improvement from baseline compared to placebo in functional measures of mobility (timed 25 walking speed; p=0.04) and lower extremity strength (manual muscle testing; p=0.01), and that the dosage curves showed increasing benefit in both measures in the 20mg to 50mg day range; no other measures showed significant improvement treatment effect" (AB Vol. 25 at p. 7828). The Poster presented by Dr. Goodman at the Baltimore conference indicated that the average improvement experienced during the low dose period (10 to 25 mg bid) included greater than 20% increase in 9 of 25 subjects (i.e. coincidentally 36% of these subjects).

[162] In his cross-examination, Dr. Leist recognized that this did provide useful information but insisted that this was not "the final word", nor was it conclusive in his view because full data is not disclosed in the Goodman Abstracts and Poster before the Federal Court. Admittedly, the very nature of these publications could not disclose what one would only find in a full report on a clinical study. But, like the Federal Court, I was taken aback by all the possible flaws (sometimes simple theoretical assumptions of what could have been done wrong during the trial) that could have an impact on the persuasiveness of the conclusion offered by the authors according to Dr. Leist. It was clearly open to the trier of fact to conclude that Dr. Leist was looking for failures.

[163] It is in that context that the Federal Court said that it accepted the conclusions as expressed by Dr. Goodman in his Abstracts and Poster as representing what a POSITA willing to understand would learn from this study (FC Decision at para. 170). Dr. Leist did not share nor accept the conclusions expressed in the Goodman reference saying that it was only the

conclusions of the authors (AB Vol. 33 at p. 9693). It was thus relevant for the trier of fact to consider that the main author of the references, Dr. Goodman, was a respected clinician who had worked for many years in this field and had years of experience in clinical trials involving MS. In fact, Dr. Goodman was part of the skilled team involved in the Schwid trial (a colleague at the time in the Department of Neurology at the University of Rochester Medical Center) in 1997 and would be alive to what could really be learned from that study. The Federal Court was not precluded from making this finding simply because Dr. Goodman was not a witness, as argued before us by the appellants.

[164] By April 2004, the POSITA would also have the safety and tolerability data of the dosages reported by Dr. Hayes. I note that this prior art is one of the few referred to in the Background section of the 277 Patent confirming its relevance (277 Patent at para 0009). As found by the Federal Court, this would be considered together with the Goodman references as being the most recent knowledge available in respect of fampridine SR. Dr. Leist admitted that by that date, based on the Hayes reference, the POSITA would know that the 17.5 bid fampridine SR composition used by Schwid would have a concentration of about 35 nanograms per ml (AB Vol. 33 at p. 9678). By that time, Acorda had also made public the fact that it had already started a larger trial—MS-F202 using the three dosages identified by Dr. Goodman as the safest: 10, 15 and 20 mg bid. The POSITA would know that Acorda, who sponsored both trials, had all the details about MSF-201 before it made that choice. On those facts and considering that the Federal Court did consider motivation as well as the conduct of the inventors, it was open to the trier of fact to reach the conclusion that it did.

[165] I will add a few comments on the course of conduct of the inventors to which the appellants say the trier of fact did not give sufficient weight. As mentioned earlier, the weight attributed to this factor (like any other) can vary according to the circumstances. In that respect, it is evident that the appellants had to establish a palpable and overriding error, for this is at the very core of the balancing of factors used by Courts to determine obviousness that I referred to at paragraph 143 above. They did not.

[166] The Federal Court considered that conduct to assess the level of efforts and difficulties that a POSITA would encounter and made a few very relevant findings. First, it accepted that *post hoc* analysis, i.e. examining the data obtained during a trial to determine why an expected result was not achieved, is commonly done following a clinical trial. Dr. Ebers said so very clearly during is his cross-examination (AB Vol. 32 at p.9256). It should be recalled that, contrary to the expectation of the team who designed this trial, none of the three dosages appeared to function as a treatment (i.e. over and above the known variations including the placebo effect not attributable to an active ingredient). Why? It only makes sense that if one is to spend time and money on a trial that one would try to understand what could be learned from it. Frankly, it is difficult to understand how anybody advanced the contrary view. I certainly do not understand either why Dr. Leist expressly limited his comment to the "average investigator" at paragraph 415 of his report, when everywhere else, he referred to the Skilled Person, and qualifies this comment again by referring to "further and unique analyses".

[167] Second, the Federal Court essentially found that by looking at a subject-by-subject data, or responses obtained during the trial (akin to n =1 mentioned by Dr. Ebers at para. 35 of his

report) or that would be obtained from a smaller trial, the POSITA could easily identify a sub-group of patients that responded to the active ingredient as opposed to known variabilities mentioned earlier in my analysis.

[168] I note in this respect that Dr. Cohen in his testimony explained that when he examined the data obtained on a subject-by-subject basis (he asked for this information that was available and easily compiled by the statistician), it took him only a few hours to identify such a group. He also said that he used his "clinical mind" to do a "clinician analysis" to identify the sub-group of patients for whom the three dosage were indeed effective (AB Vol. 28 at p. 9068-9069). This is consistent with and in fact supports the findings of the Federal Court. It is consistent with the CGK that, because of its mechanism of action, the active ingredient would only be effective as a treatment in a portion of MS patients in need thereof. There was no need after that sub-group was identified to take the further steps that were intended to persuade the FDA.

[169] There is no need to discuss the brief submissions provided by the appellants after the hearing with respect to case law involving clinical trials and their significance in the 'obvious to try 'analysis. Having reviewed them, I can discern no special or general principle applicable other than those already enunciated in *Sanofi* to which the Federal Court referred. It always remains a question of fact whether the efforts required were undue in this field where clinical trials are routinely required. I have not been persuaded that the Federal Court made a palpable and overriding error in not giving more weight to the evidence relied upon by the appellants as to the size of MSF-202. It is worth recalling that in this particular case, the mythical POSITA was

defined by the Federal Court as having experience in the design and analysis of MS trials (FC Decision at para.80).

[170] I have very carefully gone through the evidentiary record, as both parties confirmed to us at the hearing that this decision was not time sensitive. I can only conclude that the Federal Court was entitled to find that it was satisfied on a balance of probabilities that the asserted claims were invalid for obviousness. Even if in respect of some of the relevant findings the evidence may have been sparse, it is not our role to substitute the findings of the trier of fact with our own evaluation of the evidence on appeal.

[171] All this to say that I have not been persuaded that the Court made any reviewable errors that would justify our Court's intervention.

E. *Final Remarks*

[172] As mentioned, there is no need to discuss the Federal Court's findings in respect of anticipation, nor is this the proper case to address *in obiter* the question of how *Hospira Healthcare Corporation v Kennedy Trust for Rheumatology Research*, 2020 FCA 30 (*Hospira)* and the Federal Court's conclusion on anticipation might have an impact on inventions requiring investments in large clinical trials, as briefly argued.

[173] That said, it is important to recall that nothing in these reasons or my conclusion that the appeal should be dismissed, should be understood as endorsing the conclusion of the Federal

Court on anticipation. Also, neither this Court in *Hospira* nor the Federal Court intended to modify the well-established test enunciated in *Sanofi* (FC Decision at paras. 114-115).

V. Conclusion

[174] In view of the foregoing, I would dismiss the appeal and cross-appeal with costs.

"Johanne Gauthier"
J.A.

"I agree
Mary J.L. Gleason J.A."

"I agree
Marianne Rivoalen J.A."

FEDERAL COURT OF APPEAL

NAMES OF COUNSEL AND SOLICITORS OF RECORD

DOCKETS:	A-145-20 AND A-146-20

APPEAL FROM AN ORDER OF THE HONOURABLE JUSTICE MANSON DATED MAY 15, 2020, NOS. T-l163- l8 and T-220-19

DOCKET:	A-145-20
STYLE OF CAUSE:	BIOGEN CANADA INC., BIOGEN INTERNATIONAL GMBH AND ACORDA THERAPEUTICS INC. v. PHARMASCIENCE INC.
AND DOCKET:	A-146-20
STYLE OF CAUSE:	BIOGEN CANADA INC., BIOGEN INTERNATIONAL GMBH AND ACORDA THERAPEUTICS INC. v. TARO PHARMACEUTICALS INC.
PLACE OF HEARING:	OTTAWA, ONTARIO
DATE OF HEARING:	FEBRUARY 22, 2022
PUBLIC REASONS FOR JUDGMENT BY:	GAUTHIER J.A.
CONCURRED IN BY:	GLEASON J.A. RIVOALEN J.A.
DATED:	AUGUST 8, 2022

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