Federal Court  Cour fédérale

Date: 20120411

Docket: T-564-10

Citation: 2012 FC 410

Ottawa, Ontario, April 11, 2012

PRESENT: The Honourable Mr. Justice Barnes

BETWEEN:

ALCON CANADA INC.
ALCON RESEARCH, LTD. AND
KYOWA HAKKO KIRIN CO., LTD.

Applicants

and

APOTEX INC. AND
THE MINISTER OF HEALTH

Respondents

REASONS FOR JUDGMENT AND JUDGMENT

[1] This is an application by Alcon Canada Inc., Alcon Research, Ltd. and Kyowa Hakko Kirin Co., Ltd. (referred to hereafter collectively as Alcon) brought under the provisions of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133. Alcon seeks an Order prohibiting the Minister of Health (Minister) from issuing a Notice of Compliance (NOC) to Apotex Inc. (Apotex) until the expiry of Canadian Letters Patent 2,195,094 (the 094 Patent).

Background

[2] According to Alcon, the 094 Patent claims the novel use and composition of a topical ophthalmic solution containing olopatadine for treating allergic eye diseases by virtue of its previously unrecognized mast cell stabilizing activity in the human eye. In Canada, Alcon markets olopatadine under the brand name Patanol in a formulation of 0.1% olopatadine hydrochloride.

[3] Apotex has filed an Abbreviated New Drug Submission seeking a NOC from the Minister for a 0.1% ophthalmic solution of olopatadine hydrochloride for topical administration in the treatment of allergic conjunctivitis (a common disorder of the human eye).

[4] Alcon brought its application in response to a Notice of Allegation (NOA) delivered by Apotex by letter dated February 24, 2010. Apotex alleged that its generic product would not infringe the 094 Patent and, in any event, that the 094 Patent is void for anticipation, obviousness, double patenting, claims broader than the invention/lack of patentable subject matter and lack of demonstrated or predicted utility.

[5] On the record before me there is no serious issue with respect to infringement. If the 094 Patent is valid, the Apotex product will infringe.

Olopatadine and the Treatment of Human Eye Diseases as it was Known in 1995

[6] There is no material disagreement among the witnesses about the nature and physiology of human allergic eye diseases and the known methods for treating them at the relevant time.

[7] The parties are also in general agreement about the notional person of skill. Such a person could include a pharmacologist, an ophthalmologist, an immunologist or a medical doctor with an understanding of human allergy pathways and the treatment of allergic responses including an interest in the development of new treatments. The person of skill is required to interpret the 094 Patent and its claims as of the date of issuance, which in this case is December 12, 1996: see *Whirlpool Corp v Camco Inc*, 2000 SCC 67 at paras 55-56, [2000] 2 SCR 1067 [*Whirpool*].

[8] Allergic eye diseases are common disorders which affect about 10% of the population. They include allergic conjunctivitis (AC), giant papillary conjunctivitis (GPC), vernal conjunctivitis (VC), vernal keratoconjunctivitis (VKC) and atopic keratoconjunctivitis (AKC). These conditions represent aberrant immune responses where the body wrongly interprets an allergen to be an invader to be destroyed or expelled.

[9] An allergic reaction in the eye is an immunological response that arises when a previously sensitized individual is exposed to an allergen or antigen. Such a person will have formed antibodies which bind to receptors on mast cells in the eye. In this way, mast cells become sensitized and, on subsequent exposure, they degranulate, a process that releases a variety of chemical mediators including histamine. These chemical mediators are the cause of the symptoms of allergy including itching, redness, swelling and watering.

[10] While other mediators are released by mast cells including several neutral proteases, chemoattractants and interleukins, it is histamine that plays a significant role in causing allergic symptoms in the eye.

[11] Histamine exerts its effects by binding to histamine receptors. An antihistamine works by binding to those receptors thereby blocking out the histamine. This is sometimes described metaphorically as putting a false key in the lock. Antihistamines are a useful form of treatment for an allergic response but they act after the mediators are released from the mast cells and they only block the effects of one mediator – histamine.

[12] Another means of treating allergic disease is by preventing the degranulation of mast cells. This is accomplished by the administration of mast cell stabilizing agents. Mast cell stabilizers (of which olopatadine is one) act by preventing mediator release from mast cells. This form of treatment blocks the release of mediators from mast cells and is not limited to the suppression of histamine. For certain diseases, a mast cell stabilizer would be expected to be more effective than an antihistamine.

[13] In 1995, cromolyn had been identified as a mast cell stabilizer in animal models but its efficacy in humans was in doubt. It was understood at that time that animal models could usefully predict the efficacy of antihistamines in humans but not the efficacy of mast cell stabilizers. The inability to predict a mast cell stabilizing effect from animal testing was understood to arise from the problem of mast cell heterogeneity, meaning that mast cells from different species and in different tissues within the same species were sufficiently different that a compound's efficacy in one would not predict efficacy in another.

[14] For several years leading up to 1995, there was a recognized need for mast cell stabilizers useful to treat some forms of allergic eye disease. In reaction to that need, Alcon initiated a search for a compound that was both a mast cell stabilizer and an antihistamine. By 1995, the 094 Patent inventors and others working in the field believed that antihistamines were unlikely to be useful as mast cell stabilizers because, in vitro and at higher concentrations, they were observed to rupture the cell causing unwanted release of mediators (the biphasic effect) – a result that was opposite to the desired stabilization effect.

[15] One of the 094 Patent inventors, Dr. John Yanni, and another colleague at Alcon developed a novel assay which was the first available method to test a drug for mast cell stabilization in the human conjunctival mast cell (the HCMC assay). The HCMC assay later formed the subject matter of a United States patent application filed on October 8, 1993.

[16] Dr. Yanni set out to test approximately 150 compounds with the HCMC assay. Many of the compounds obtained by Alcon came from other companies under transfer agreements and were known to have anti-allergic profiles. Alcon obtained olopatadine in this way from Kyowa Hakko Kirin Co., Ltd. (Kyowa) in 1991 because it was known to be an antihistamine useful in treating allergic eye diseases in humans. Dr. Yanni understood olopatadine to be an antihistamine and was concerned that it could exhibit a biphasic effect. Upon testing olopatadine, it was discovered to have mast cell stabilizing properties at certain doses and that this response was dose dependent. At therapeutic doses, olopatadine was found not to be biphasic.

[17] In 1997, Alcon brought olopatadine to market under the trade name Patanol and this product has achieved considerable commercial success for the treatment of allergic eye diseases.

Analysis

[18] The outcome of this application turns on claims construction. This is an issue of law for the Court to determine but with the aid of expert witnesses: see *Pfizer Canada Inc v Canada (MOH)*, 2007 FCA 209 at para 39, [2007] FCJ no 767 (QL).

[19] The issue of burden of proof in NOC proceedings has now been settled and I adopt the following analysis provided by Justice Roger Hughes in the *Eli Lilly Canada Inc v. Apotex Inc*, 2009 FC 320 at paras 37-40, 346 FTR 78:

> 37 The issue as to who bears the burden of proof in NOC proceedings, as to validity of a patent or infringement of a patent is an issue that I had thought had been put to rest. Nonetheless the parties in such proceedings continue to argue the point. It seems that my recent decision in *Brystol-Myers Squibb Canada Co. v. Apotex Inc.*, 2009 FC 137 has given fresh ammunition to those continually wishing to stir the pot in this regard. Let me state emphatically that I did not intend in *Brystol-Myers* to say or apply any burden different than I had stated in previous decisions.
>
> 38 To be perfectly clear, when it comes to the burden as to invalidity I canvassed the law, in particular recent Federal Court of Appeal decisions, in *Pfizer Canada Inc. v. Canada (Minister of Health)*, (2008), 69 C.P.R. (4th) 191, 2008 FC 11 and concluded at paragraph 32:
>
> > *32 I do not view the reasoning of the two panels of the Federal Court of Appeal to be in substantial disagreement. Justice Mosley of this Court reconciled these decisions in his Reasons in Pfizer Canada Inc. v. Apotex Inc., [2007] F.C.J. No. 1271, 2007 FC 971 at paragraphs 44 to 51. What is required, when issues of validity of a patent are raised:*

> *1. The second person, in its Notice of Allegation may raise one or more grounds for alleging invalidity;*
>
> *2. The first person may in its Notice of Application filed with the Court join issue on any one or more of those grounds;*
>
> *3. The second person may lead evidence in the Court proceeding to support the grounds upon which issue has been joined;*
>
> *4. The first person may, at its peril, rely simply upon the presumption of validity afforded by the Patent Act or, more prudently, adduce its own evidence as to the grounds of invalidity put in issue.*
>
> *5. The Court will weigh the evidence; if the first person relies only on the presumption, the Court will nonetheless weigh the strength of the evidence led by the second person. If that evidence is weak or irrelevant the presumption will prevail. If both parties lead evidence, the Court will weigh all the evidence and determine the matter on the usual civil balance.*
>
> *6. If the evidence weighed in step 5 is evenly balanced (a rare event), the Applicant (first person) will have failed to prove that the allegation of invalidity is not justified and will not be entitled to the Order of prohibition that it seeks.*

39 I stated the matter more succinctly in *Pfizer Canada Inc. v. Canada (Minister of Health)*, 2008 FC 500 at paragraph 12:

> *12 Here the only issue is validity. Pharmascience has raised three arguments in that respect. Each of Pfizer and Pharmascience have led evidence and made submissions as to those matters. At the end of the day, I must decide the matter on the balance of probabilities on the evidence that I have and the law as it presently stands. If, on the evidence, I find that the matter is evenly balanced, I must conclude that*

> *Pfizer has not demonstrated that Pharmascience's allegation is not justified.*
>
> 40 The above cases state correctly in my view, the law as to the burden in NOC proceedings as to invalidity.
>
> [Emphasis in original]

[20] Alcon asserts only two of the 25 claims of the 094 Patent, specifically Claim 8 (a use claim) and Claim 20 (a composition claim) but it acknowledges that, as dependant claims, they must be read in the context of the claims to which they are linked (ie. Claims 1 and 13 respectively). For ease of reference all of the 094 Patent claims are set out below:

> CLAIMS:
>
> 1. Use of a topically administrable ophthalmic composition comprising a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier therefor, for treating allergic eye diseases.
>
> 2. The use of Claim 1, wherein the composition is a solution and the amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.0001% to about 5% (w/v).
>
> 3. The use, of Claim 2, wherein the amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is about 0.001% to about 0.2% (w/v)
>
> 4. The use of Claim 3, wherein the amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is about 0.1% (w/v).
>
> 5. The use of Claim 1, wherein the 11-(3-dimethylamino-propylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz [b,e] - oxepin-2-acetic acid, substantially free of (E)-11-(3-dimethyl-aminoproylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid.

6. The use of Claim 5, wherein the amount of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.0001 to about 5% (w/v).

7. The use of Claim 6, wherein the amount of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.001 to about 0.2% (w/v).

8. The use of Claim 7, wherein the amount of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is 0.1% (w/v).

9. The use of Claim 1, wherein the 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid, substantially free of (Z)-11-(3-dirnethylarninopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid.

10. The use of Claim 9, wherein the amount of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.0001 to about 5% (w/v).

11. The use of Claim 10, wherein the amount of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.001 to about 0.2% (w/v).

12. The use of Claim 11, wherein the amount of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is about 0.1% (w/v).

13. A topically administrable ophthalmic composition for treating allergic eye diseases comprising a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier therefor.

14. The composition of Claim 13 wherein the amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.0001 to about 5% (w/v).

15. The composition of Claim 14 wherein the amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.001 to about 0.2% (w/v).

16. The composition of Claim 15 wherein the amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodlbenz[b,e]oxepin-2-acetic acid is about 0.1% (w/v).

17. The composition of Claim 13 wherein the 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid, substantially free of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodlbenz[b,e]oxepin-2-acetic acid.

18. The composition of Claim 17 wherein the amount of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.0001 to about 5% (w/v).

19. The composition of Claim 18 wherein the amount of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.001 to about 0.2% (w/v).

20. The composition of Claim 19 wherein the amount of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is about 0.1% (w/v).

21. The composition of Claim 13, wherein the 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid, substantially free of (Z)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid.

22. The composition of Claim 21, wherein the amount of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz [b,e]oxepin-2-acetic acid is from about 0.0001 to about 5% (w/v).

23. The composition of Claim 22, wherein the amount of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is from about 0.001 to about 0.2% (w/v).

24. The composition of Claim 23, wherein the amount of (E)-11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid is about 0.1% (w/v).

25. Use of a composition as defined in any one of claims 13 to 24 for the preparation of a medicament for treating allergic eye diseases.

[21] It is the language of Claims 1 and 13 that is disputed by the parties and, in particular, the words "treating" and "allergic eye diseases".

[22] Because olopatadine was a known antihistamine useful for treating human allergic eye diseases, Apotex maintains that, on a plain reading, the 094 Patent asserts a monopoly over a known compound for an old use. Alcon concedes that, if this interpretation is adopted, the 094 Patent will fail on the ground of obviousness.

[23] Alcon argues that the 094 Patent claims a novel use of olopatadine in the treatment of allergic eye diseases by virtue of the discovery of its previously unrecognized mast cell stabilizing activity in the human eye. Alcon urges a contextual interpretation of the words "treating" and "allergic eye diseases" which effectively reads into Claims 1 and 13 a limitation related to the discovery of olopatadine's usefulness as a mast cell stabilizer and an antihistamine to treat diseases of the human eye where mast cell degranulation is implicated. Alcon alleges that this is in keeping with the spirit of what the 094 Patent disclosed. Accordingly, Alcon advances the following construction of Claims 8 and 20:

> 1) a composition tailored for use in an ocular environment and to be applied to the surface of the eye;
>
> 2) containing olopatadine (or one of its pharmaceutically acceptable salts);
>
> 3) having less than 2% of the trans-isomer of olopatadine present;
>
> 4) the concentration of olopatadine being 0.1% (w/v); and
>
> 5) <u>having clinically relevant HCMC stabilizing activity and antihistaminic activity (i.e. a 'dual action agent') for prophylactic and therapeutic treatment in human of an</u>

> allergic eye disease wherein mast cell degranulation contributes to the development of the disease state (such as AC, VC, VKC and GPC).
>
> [Emphasis added]
>
> Applicant's Outline of Argument – Construction at para 53.

[24] Although the parties agree that the construction of patent claims must be carried out purposively and in accordance with the principles discussed in *Whirlpool*, and *Free World Trust v Électro Santé Inc*, 2000 SCC 66, [2000] 2 SCR 1024 [*Free World*], they disagree about how far one can go in construing claims language on the strength of information that is provided only in the disclosure. Alcon argues that the skilled reader must draw meaning from the entire context of a patent. Apotex says a purposive contextual reading does not permit the claims to be rewritten to include missing essential elements.

[25] Claims language is a critical component of the public notice requirement and subsection 27(4) the *Patent Act*, RSC 1985, c P-4,, emphasizes its importance:

> 27. (4) The specification must end with a claim or claims defining distinctly and in explicit terms the subject-matter of the invention for which an exclusive privilege or property is claimed.

[26] The Supreme Court of Canada emphasized the purpose and importance of requiring clear language in the drafting of patent claims in *Free World*, above, at paragraphs 14, 15 and 42:

> 14 Patent claims are frequently analogized to "fences" and "boundaries", giving the "fields" of the monopoly a comfortable pretence of bright line demarcation. Thus, in Minerals Separation North American Corp. v. Noranda Mines, Ltd., [1947] Ex. C.R. 306, Thorson P. put the matter as follows, at p. 352:

> By his claims the inventor puts fences around the fields of his monopoly and warns the public against trespassing on his property. His fences must be clearly placed in order to give the necessary warning and he must not fence in any property that is not his own. The terms of a claim must be free from avoidable ambiguity or obscurity and must not be flexible; they must be clear and precise so that the public will be able to know not only where it must not trespass but also where it may safely go.

15 In reality, the "fences" often consist of complex layers of definitions of different elements (or "components" or "features" or "integers") of differing complexity, substitutability and ingenuity. A matrix of descriptive words and phrases defines the monopoly, warns the public and ensnares the infringer. In some instances, the precise elements of the "fence" may be crucial or "essential" to the working of the invention as claimed; in others the inventor may contemplate, and the reader skilled in the art appreciate, that variants could easily be used or substituted without making any material difference to the working of the invention. The interpretative task of the court in claims construction is to separate the one from the other, to distinguish the essential from the inessential, and to give to the "field" framed by the former the legal protection to which the holder of a valid patent is entitled.

…

42 The patent system is designed to advance research and development and to encourage broader economic activity. Achievement of these objectives is undermined however if competitors fear to tread in the vicinity of the patent because its scope lacks a reasonable measure of precision and certainty. A patent of uncertain scope becomes "a public nuisance" (R.C.A. Photophone, Ld. v. Gaumont-British Picture Corp. (1936), 53 R.P.C. 167 (Eng. C.A.), at p. 195). Potential competitors are deterred from working in areas that are not in fact covered by the patent even though costly and protracted litigation (which in the case of patent disputes can be very costly and protracted indeed) might confirm that what the competitors propose to do is entirely lawful. Potential investment is lost or otherwise directed. Competition is "chilled". The patent owner is getting more of a monopoly than the public bargained for. There is a high economic cost attached to uncertainty and it is the proper policy of patent law to keep it to a minimum.

[27] Notwithstanding the above cautions, the law is clear that a purposive approach requires the Court to examine claim language in the sense that the patentee is presumed to have used it and not through the lens of strict literalism. Even a term that appears to be plain and unambiguous may, when read in the context, reasonably support a different meaning. *Whirlpool*, above, also counsels that the search for meaning is not carried out through the eyes of a grammarian but rather in light of the common knowledge of the person of ordinary skill in the field to which the patent relates. Thus, it is permissible to look to the patent disclosure to ascertain the technical meaning of terms used in the claims.

[28] I have no difficulty with the point that purposive construction is capable of expanding or limiting a literal text: see *Whirlpool*, above, at para 49. It seems to me, though, that there is some judicial concern about importing essential features of an invention from the disclosure to the claims, particularly where the disclosure is somewhat unclear about the scope of the invention. In other words, even if one resorts to the disclosure to interpret the claims "the precise and exact extent of the exclusive property and privileged claims" must always be identifiable: see *Consolboard Inc v MacMillan Bloedel (Saskatchewan) Ltd*, [1981] 1 SCR 504 at para 26, 122 DLR (3d) 203.

[29] In *BVD Co v Canadian Celanese Ltd*, [1937] SCR 441, [1937] 3 DLR 449 [*BVD*], the Court declined to read into a patent claim an essential feature of an invention and struck the patent down because the claims, as written, exceeded the scope of the invention. I take Alcon's point that this decision predates the decisions in *Whirlpool* and *Free World*, above, and their elaboration of the principles of purposive construction. Nevertheless, *BVD* has not been overruled and it continues to underscore the importance of ensuring that a patent clearly delineates the subject matter of an

invention and the importance of the claims language in achieving that end: see also *Apotex Inc v Sanofi-Synthelabo Canada Inc*, 2008 SCC 61 at para 77, [2008] 3 SCR 265; *Amfac Foods Inc v Irving Pulp & Paper, Ltd*, [1986] FCJ no 659 (QL), 72 NR 290 (CA).

[30] What I take from the authorities is that resort to the disclosure is permissible, but only for the purpose of comprehending the meaning of words or expressions found in the claims. Essential information that is contained in the disclosure that is not relevant to the search for meaning of claims language cannot be imported by implication to qualify the claims: see *Janssen-Ortho Inc v Canada (MOH)*, 2010 FC 42 at para 119, 361 FTR 268 [*Janssen-Ortho*]. It is also not appropriate to ascribe meaning to words in the claims by reference to "stray phrases" found in the disclosure: see *Electric & Musical Industries, Ltd v Lissen, Ltd* (1939), 56 RPC 23 at p 41.

[31] The first step in a patent suit is to construe the claims without regard to issues of validity or infringement: see *Whirlpool*, above, at para 43. Where there is doubt about the meaning of claims language, one resorts first to the language of the claims followed by consideration of the disclosure, if necessary: see *Janssen-Ortho*, above, at para 116.

[32] Alcon argues that a person of skill would, at the relevant time, understand that the 094 Patent claims a new use for olopatadine in the treatment of allergic eye diseases owing to its discovered activity as a mast cell stabilizer in addition to its already known value as an antihistamine.

[33] Alcon acknowledges that on a plain reading of the claims in issue the use of olopatadine to treat allergic eye diseases exceeds the scope of its invention. By resorting to the disclosure, Alcon seeks to read down this expansive language and to restrict the claims to "clinically relevant HCMC stabilizing activity and antihistaminic activity (ie. a 'dual action agent') for prophylactic and therapeutic treatment in a human of an allergic eye disease wherein mast cell degranulation contributes to the development of the disease state (such as AC, VC, VKC and GPC)": Applicant's Outline of Argument – Construction at para 53.

[34] The passages in the 094 Patent disclosure that Alcon's witnesses rely upon to read down the language of the claims include the following:

> The present invention relates to topical ophthalmic formulations used for treating allergic eye diseases, such as allergic conjunctivitis, vernal conjunctivitis, vernal keratoconjunctivitis, and giant papillary conjunctivitis. More particularly, the present invention relates to therapeutic and prophylactic topical use of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid for treating and/or preventing allergic eye diseases.
>
> …
>
> Topical ophthalmic formulations which contain drugs having conjunctival mast cell activity may only need to be applied once every 12-24 hours instead of once every 2-4 hours. One disadvantage to the ophthalmic use of reported anti-allergic drugs which in fact have no human conjunctival mast cell stabilizing activity is an increased dosage frequency. Because the effectiveness of ophthalmic formulations containing drugs which do not have conjunctival mast cell activity stems primarily from a placebo effect, more frequent doses are typically required than for drugs which do exhibit conjunctival mast cell activity.
>
> …
>
> What is needed are topically administrable drug compounds which have demonstrated stabilizing activity on mast cells obtained from human conjunctiva, the target cells for treating allergic eye

> diseases. What is also needed are local administration methods for the treatment of allergic eye disease.
>
> …
>
> The present invention provides a method for treating an allergic eye disease characterized by administering to the eye a topical ophthalmic formulation which contains a therapeutically effective amount of 11-(3-dimethylaminopropylidene)-6, 11-dihydrodibenz[b,e]oxepin-2-acetic acid (referred to as "Compound A" hereinafter) or a pharmaceutically acceptable salt thereof.
>
> …
>
> Compound A has human conjunctival mast cell stabilizing activity, and may be applied as infrequently as once or twice a day in some cases. In addition to its mast cell stabilizing activity, Compound A also possesses significant antihistaminic activity. Thus, in addition to a prophylactic effect, Compound A will also have a therapeutic effect.
>
> …
>
> As Table 1 clearly shows, the anti-allergic drugs disodium cromoglycate and nedocromil failed to significantly inhibit human conjunctival mast cell degranulation. In contrast, Compound A (*cis* isomer) [olopatadine] produced concentration-dependent inhibition of mast cell degranulation.

[35] Alcon and its opinion witnesses maintain that the above passages would lead a person of skill to understand that the claims in question did not include the use of olopatadine generally to treat allergic eye diseases. The disclosure is all about olopatadine's capacity to stabilize mast cells in the human eye and its use to treat diseases where mast cell degranulation is a concern. In addition, Alcon contends that part of the inventive utility of olopatadine lies in its potential use as a dual action prophylactic agent. Alcon also relies on prior art disclaimers in the 094 Patent disclosure that, it says inform a skilled reader about what is not included in the claims.

[36] Alcon urges an interpretation of the word "treating" in Claim 1 that is consistent with its characterization of olopatadine's mast cell stabilizing activity as a new medical use. According to Alcon, the skilled reader would understand that, when read in context, "treating" is not being used in a general sense and must mean more than the use of olopatadine as an antihistamine. Alcon also argues that the use of olopatadine to treat allergic eye diseases as a mast cell stabilizer does not inherently involve treatment as an antihistamine because the dosage ranges for each method of treatment do not overlap. Using olopatadine to prophylactically treat allergic eye diseases is, therefore, distinct from its understood antihistaminic utility.

[37] Alcon similarly urges a narrow interpretation of the words "allergic eye diseases" which, it argues, do not include disorders that cannot be treated with a mast cell stabilizer. This would be obvious to the skilled person because the list of treatable eye diseases in the specification includes only four examples where, in each case, mast cell degranulation is implicated at least to some extent. Alcon argues that this unstated common feature should, accordingly, be read into the relevant claims.

[38] At the outset, it is important to recognize that nowhere in the claims is there any mention of a newly discovered and inventive use for olopatadine. There is also no reference in the claims to any particular activity or to a dual activity which might restrict the claimed use of olopatadine. While these activity profile features are described in the disclosure and quantified with respect to olopatadine's mast cell stabilizing property, those references are similarly not tied to any new form of clinical use. Indeed, the summary of the invention refers to a method for treating and not to a use. This appears to conform to the United States priority patent which claimed a method of

medical treatment based on olopatadine's mast cell stabilizing properties. And despite Alcon's considerable reliance in argument on olopatadine's dual action profile and the avoidance of a biphasic effect, there is nothing in the specification to suggest that these features are part of the inventive promise of the 094 Patent.

[39] The disclosure passages Alcon relies upon also fail to clearly identify the nature or the scope of the invention. There is nothing in these passages which distinctly and explicitly identifies the subject matter of the invention whether as a new use or otherwise. While there are references to prophylactic use, dosing frequencies and demonstrated stabilization activity at specific concentrations, none of those features are clearly identified as an element of the inventive concept and none of that language is used in a way that would serve to clearly define the words in dispute in Claims 1 and 13.

[40] Furthermore, with respect to Alcon's reliance on a distinction between prophylactic and therapeutic uses, the language it has used is notably imprecise. For example, there are places in the disclosure where therapeutic and prophylactic uses for olopatadine are distinguished: therapeutic use is said to treat and prophylactic to prevent. But in other places, the word "treating" is used in the general sense without distinguishing the means by which the clinical outcome is achieved and "therapeutic" refers to a dosage (see Claim 1 and Claim 13).

[41] This linguistic inconsistency is mirrored by the evidence. According to Alcon's own witnesses, there is no bright clinical line that ordains the use of olopatadine as a preventative therapy.[1]

[42] The plain reading of Claim 1 is that olopatadine can be used to treat a broader class of allergic eye diseases than the four examples provided in the disclosure and, of course, there is no express statement anywhere in the patent that the claims are limited to the treatment of disorders where mast cell degranulation is implicated. The disclosure is open-ended in that respect.

[43] The evidence from Alcon's witnesses concerning the disputed claims language is not particularly helpful because it is based on disclosure references that are not clear. Those witnesses also failed to address other disclosure references that detracted from their views and they attributed an awkward meaning to "treating" that seems to be more consistent with Alcon's legal interests than with the objective views of a skilled reader.

[44] Dr. Church provided the following affidavit evidence on these construction issues:

> 62. What is meant by the phrase "treating allergic eye diseases" as used in the claims of the 094 Patent would be readily discerned by the skilled person based on a review of the 094 Patent in its entirety. As discussed earlier, page 4, lines 11-13 of the patent refers to "treating allergic eye diseases" in a context of helping target cells, i.e., human conjunctival mast cells. The passage states that what is needed is a drug that has demonstrated stabilizing activity on mast cells obtained from human conjunctiva, the target cells for treating allergic eye diseases. Hence, a skilled person would understand that "treating" involves stabilizing human conjunctival mast cells (i.e., preventing human conjunctival mast cell degranulation) to a

[1] Dr. Barney acknowledged that antihistamines could be used preventatively (see Cross-Examination of Dr. Neal P. Barney (M.D.) (21 September 2011) at p 104.) and Dr. Church accepted that mast cell stabilizers could be used symptomatically (see Cross-Examination of Dr. Martin K. Church (7 September 2011) at p 75

> significant level. The phrase "allergic eye diseases" would have been understood to mean those diseases in which conjunctival mast cell degranulation is involved, at least in part. On page 1, 11. 10-12 the patent provides some examples of such types of "allergic eye diseases". That passage states that "the present invention relates to topical ophthalmic formulations used for treating allergic eye such as allergic conjunctivitis, vernal conjunctivitis, vernal keratoconjunctivitis, and giant papillary conjunctivitis." Given that a common feature of these diseases is that, as at December, l996, they were thought to have mast cell degranulation as all or part of the disease state, the skilled person would have construed "allergic eye disease" to mean diseases in which mast cell degranulation is involved.
>
> 63. While some of the diseases referred to as "allergic eye diseases" would not be "cured" by mast cell stabilization, the skilled person would nonetheless appreciate that the diseases would be "treated" (perhaps even as an adjunct therapy) by mast cell stabilization.
>
> 64. The "treatment" by stabilizing human conjunctival mast cells would have been understood by the skilled person to be an added activity over the previously known antihistaminic activity of Compound A. Hence the skilled person would understand that the word "treating" in the phrase "treating allergic eye diseases" means prophylactically and/or therapeutically treating allergic eye diseases in humans by stabilizing human conjunctival mast cells in a manner that is significant in addition to having antihistaminic activity. The inventive concept of the claims is that Compound A can be used topically at clinically relevant concentrations to prevent histamine release from the mast cells in human conjunctiva in addition to its known antihistaminic activity.
>
> See also Affidavit of Martin K. Church, Ph.D., D.Sc. (31 May 2011) at paras 5-7: Affidavit of Phil Lieberman (19 January 2011) at paras 81, 83, 92 [Affidavit of Dr. Lieberman].

Dr. Lieberman's affidavit addresses the same point at paragraph 172:

> 172. At paragraphs 78, 79 and 85 of his affidavit, Dr. Buckley suggests the 094 Patent describes a mechanism of action for olopatadine rather than a new use. I disagree. The use claimed in the 094 Patent is a new use, because it was never used before to treat human eye allergy or as a human conjunctival mast cell stabilizer.

> "Treating" as used in the claims, means apart from being an anti-histamine, also being a significant conjunctival mast cell stabilizer.
>
> Affidavit of Dr. Lieberman at para 172.

[45] This evidence equates the word "treating" with the way in which olopatadine works (eg. "helping target cells", "'treating' involves stabilizing human conjunctival mast cells", "'treated' by…mast cell stabilization"). Except for a reference to a possible use as a prophylaxis, Dr. Church and the other Alcon witnesses identify no new clinical use for olopatadine that arises out of the discovery of its mast cell stabilizing properties beyond the sophism that if olopatadine was never used before as a mast cell stabilizer it therefore must be a new use. It seems to me that this approach seriously strains the meaning of the word "treating" and the concept of a new use discovery. The information discovered by Alcon may be useful but it does not, by that fact alone, constitute a new use for olopatadine. A clinician treats a patient for an allergic reaction in the eye by suppressing the troubling or damaging signs and symptoms of the disorder. In the absence of a new clinical use for an old drug, new knowledge about how it works is not patentable. Similarly, the discovery that olopatadine was more effective in the treatment of allergic eye diseases than initially understood (see Affidavit of Martin K. Church, Ph.D., D. Sc. (24 January 2011) at paras 42-43, 46-48 [Affidavit of Dr. Church]) is unpatenable because the improved efficacy of the drug was inherent in its known utility as an antihistamine: see *AztraZeneca AB v Apotex Inc*, 2007 FC 688 at paras 50-52, 80-88, 314 FTR 177.

[46] The evidence from the Apotex witnesses that "treating" means the therapeutic alleviation of the signs and symptoms of allergic eye diseases without regard to any mechanism of action is in

keeping with the plain language of Claim 1 and it avoids an unnatural equating of the word to olopatadine's biological activity as a mast cell stabilizer.

[47] Alcon maintains that Dr. Buckley and Dr. Calder retreated from their respective affidavits under cross-examination and conceded that Claim 1 incorporated, by implication, the use of olopatadine as a mast cell stabilizer. I do not agree that either witness made such an unqualified concession. Dr. Buckley's answers were given in response to questions relating to references in the disclosure to the prophylactic and therapeutic effects of olopatadine but, under further questioning, he stated that the 094 Patent "claims to treat and prevent perhaps, but without claiming the pathway or the pharmacological mechanisms": Cross-Examination Upon Oral Examination of Dr. Roger Buckley (16 August 2011) at p 43 [Cross-Examination of Dr. Buckley]. Inasmuch as Dr. Barney conceded that antihistamines can be used in preventative ways, this evidence is not particularly probative.

[48] Dr. Calder's evidence under cross-examination is also not as clear as Alcon asserts. Much of the evidence Alcon relies upon from Dr. Calder is concerned with statements from the 094 Patent disclosure and not from the claims *per se*. Furthermore, much of that questioning was concerned with the "inventive concept" of the patent and not with the word "treating" in Claim 1. Her apparent acknowledgement that the list of exemplar diseases in the disclosure implied a use of olopatadine "as more than simply an antihistamine" does not, to my mind, detract from her evidence that "treating" in Claim 1 does not mean treating as a mast cell stabilizer or as a dual action agent. I do not take her answers under cross-examination to be inconsistent with her affidavit that Claims 1 and 13 are not limited to the use of olopatadine as a mast cell stabilizer or as a dual action medicine.

[49] Alcon maintains that "allergic eye diseases" should also be read-down by limiting the claim to diseases which implicate mast cell degranulation. I accept the point made by Alcon's expert witnesses that a skilled person may understand without being told that each of the diseases specified in the disclosure involves, in some measure, mast cell degranulation. It does not follow, however, that such a person would read that limitation into the claims. Indeed, it is inconceivable to me that the draftsman would fail to incorporate any reference to this essential limiting element in both the claims and the disclosure and thereby leave the point to be inferred by the reader. Alcon's failure to close the category of diseases amenable to treatment with olopatadine implies just the opposite – that is, that the use of olopatadine was being claimed without any limitation beyond the general reference to the treatment of allergic eye diseases. Contrary to Dr. Barney's affidavit at paragraph 47, the 094 Patent is notably unclear if the intention was to include Alcon's proposed limitation. This is particularly the case for diseases like AKC where mast cell degranulation is only a part of the disease pattern and where olopatadine would only be an incidental or adjunct form of therapy: see Cross-Examination of Dr. Buckley at pp 1805-1808; Affidavit of Dr. Church at para 63. This points away from the idea that a skilled person would infer that the 094 Patent claims are limited to the treatment of allergic eye diseases involving mast cell degranulation.

[50] The evidence before me provides no basis for ignoring the otherwise plain language of Claims 1 and 13 and, in my view, it would almost never be appropriate to limit the language of a patent claim on the strength of such an inference to be drawn from the disclosure.

[51] It would have been a simple exercise to state Alcon's suggested limitation and to clearly limit the monopoly to the use of olopatadine as a mast cell stabilizer in the treatment of diseases where mast cell degranulation was a clinical concern. It is not reasonable to read in these limitations based on an inference to be drawn from an unstated common feature of the exemplar diseases particularly where olopatadine was a known antihistamine and could also be used on its own or as adjunct therapy in the treatment of the same allergic eye diseases. This is particularly evident when one considers that several of the 094 Patent claims refer to dosages of olopatadine that, according to the experimental data set out in Table 1, would not be effective to achieve any mast cell stabilizing effect. Although Alcon does not assert any of those problematic claims in this proceeding, the skilled reader is trying to interpret all of the claims in context and not in isolation. The inference that would reasonably be drawn by the skilled reader is that Alcon was claiming the use of olopatadine as something other than a mast cell stabilizer at those lower dosage levels.

[52] The requirement that the subject matter of an invention be distinctly and explicitly defined is not met in these circumstances. A patentee should not readily be permitted to discourage competition with an overbroad claim and, when challenged many years later, retreat from the language it has used by relying on inferences and disclosure references such as these.

[53] Alcon relies on disclaimers in the 094 Patent in support of its argument that that which is disclaimed is not claimed: see *Virgin Atlantic Airways Ltd v Premium Aircraft Interiors UK Ltd*, [2009] EWCA Civ 1062 at para 21, [2010] RPC 8.

[54] The 094 Patent does acknowledge the prior art teachings of two Burroughs Wellcome (BW) patents and a Kyowa patent but at the same time substantially discounts their significance. For instance, the BW patents are said to have disclosed olopatadine's antihistaminic "activity" and an ophthalmic solution formulation, but the claim for human medical use was said not to have been established by the animal testing disclosed.[2] The 094 Patent then goes on to state that the further assertion in the BW patents that olopatadine could be classified as a mast cell stabilizer was unproven because of the problem of mast cell heterogeneity. The Kyowa Patent is characterized in a similar way in the 094 Patent by questioning the utility of olopatadine for treating the human eye. According to Alcon, the field was open to establish olopatadine's utility as a mast cell stabilizer in the human eye.

[55] I agree with Apotex that the scope of Alcon's disclaimer is far from clear and provides less than what was actually known about olopatadine. Alcon now says in its Memorandum that the 094 Patent contains no criticism of the BW teaching that olopatadine had antihistaminic "activity" and that the skilled person was being told that olopatadine was an antihistamine available for the treatment of allergic eye diseases in humans. This submission, however, goes well beyond the scope of what the 094 Patent actually acknowledged about the prior art. On one reading of the disclosure, the impression is left that the utility of olopatadine as an antihistamine, at least for human use, was unproven and that Alcon had shown that it "possesses significant antihistaminic activity". Nowhere in the 094 Patent is there an unequivocal acknowledgment that olopatadine was

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[2] Notwithstanding Dr. Calder's apparently different view, the 094 Patent is markedly unclear about what the BW Patents had supposedly demonstrated as can be seen in the following passage: "Although both of the Burroughs Wellcome Patents claim that the variety of pharmaceutical formulations disclosed are effective both for veterinary and for human medical use, neither patent contains an example demonstrating that the carboxylic acid derivatives of doxepin have activity in humans. Example 7 in the Burroughs Wellcome Patents demonstrates antihistamine activity in male guinea pigs and Example G demonstrates anaphylactoid activity in Wistar rats." [Emphasis added] This is followed immediately by a discussion about the problem of mast cell heterogeneity.

a known antihistamine available for use in the human eye or that animal testing was known to be predictive of olopatadine's antihistaminic efficacy in humans.

[56] In my view, the skilled reader would not infer from these incomplete prior art disclaimers that Alcon was limiting the word "treating" to uses which were intrinsic to mast cell stabilization and disclaiming olopatadine's use as an antihistamine. The failure to make an unequivocal disclaimer with respect to olopatadine's antihistaminic utility supports the interpretation that Alcon was attempting to claim the use of olopatadine generally to treat human allergic eye diseases through Claim 1.

[57] Alcon says that olopatadine's utility as a mast cell stabilizer is not inherent in its use as a simple antihistamine because it is only at dosages that far exceed what would be necessary for antihistaminic use that its mast cell stabilizing effects would occur. The 094 Patent does not, however, inform the reader of this distinction or instruct on how one could avoid an infringement by this means. Instead, the presence of several other claims in the 094 Patent for the use of olopatadine to treat allergic eye diseases at concentrations much lower than 0.1% belie Alcon's interpretation. There is also evidence from the prior art that indicates that antihistamines can be effectively used at dosages equivalent to 0.1%: see Affidavit of Ines Ferreira, Exhibit "B.11" at p 668. Alcon's witnesses conceded that, at such a dosage, a clinician had no control over olopatadine's biological activity: see Cross-Examination of Dr. Martin K. Church (7 September 2011) at p 77; Cross-Examination of Dr. Neal P. Barney, M.D. (21 September 2011) at pp 41-44 [Cross-Examination of Dr. Barney]; Cross-Examination of Phil Lieberman, M.D. (2 October 2011) at pp 86-88.

[58] In their affidavits, the Alcon witnesses attempted to link the discovery of olopatadine's mast cell stabilization properties to its supposedly novel clinical utility as a prophylactic agent. Although there is a reference in the disclosure to the therapeutic and prophylactic use of olopatadine, there is nothing to indicate that this was a newly discovered and inventive utility. Instead, Claims 8 and 20 refer to a therapeutically effective amount of olopatadine and none of the claims refer to a prophylactic utility.

[59] Alcon's witnesses did not strongly assert that the inventive concept lay in the use of olopatadine as a prophylactic agent. For example, Dr. Barney agreed under cross-examination that antihistamines could also be used in advance to prevent the appearance of allergic symptoms: see Cross-Examination of Dr. Barney at pp 104-107. His lack of comfort in placing reliance on olopatadine's utility as a prophylaxis can also be seen in the following exchanges under cross-examination:

> 389 Q. Let me show you an article. I have a copy for you and Mr. Belmore. It's entitled, "Conjunctival Mast Cells in Ocular A1lergic Disease," and you recognize that article, I take it?
>
> A. Yes.
>
> 390 Q. And look at Page 121 of your paper. Right column, you wrote,
>
> > "For the majority of individuals with ocular allergy, topical application of mast cell stabilizing antihistamine drugs are effective in relieving the symptoms of immediate hypersensitivity, redness, itching, tearing,"
>
> Do you see that?
>
> A. Yes.
>
> 391 Q. And in this portion of your article, despite talking about mast cell stabilizing effects -- despite talking about mast cell

stabilizing medicines, you speak about the relief of symptoms, do you see that?

A. Yes.

392 Q. And what you wrote in your article, I presume. was believed by you to be accurate when you wrote it?

A. Yes.

393 Q. And you knew mast cell stabilizers also, at least you believed mast cell also had prophylactic effects, correct?

A. Well, prophylactic in that I believe they have mast cell stabilization effect. I'm not sure how that means prophylactic.

394 Q. So your use of the term symptomatic in your article didn't rule out the possibility of the drug acting as mast cell stabilizers, correct?

A. That's correct.

…

479 Q. My question was do you think that Claim 1 embraces prophylactic use, yes or no?

MR. BELMORE: He has given you his answer in terms of inhibition of release of antihistamine mediators.

480 Q. That wasn't my question. It was something that he was eager to tell me, but my question was whether or not you construe the claim to embrace prophylactic uses.

A. It doesn't say prophylactic, and I would take from this that it's capable of diminishing signs and symptoms of allergy.

481 Q. And that would be so for all of the claims of the patent? Take your time to look at them.

A. All of the claims relate to Claim 1.

[Emphasis added]

Cross-Examination of Dr. Barney at pp 85-86, 109.

[60] On the strength of this evidence and the equivocal and imprecise use of the terms "therapeutic" and "prophylactic" in the disclosure, I do not accept that this term can be read into the claims as Alcon maintains.

Conclusion

[61] For the foregoing reasons Alcon's construction of the patent claims in issue is rejected. Because the 094 Patent purports to claim a monopoly over olopatadine for its known utility for the treatment of allergic eye diseases it fails on the ground of obviousness. The 094 Patent is invalid and Alcon's application for an order prohibiting the Minister from issuing a NOC to Apotex is dismissed with costs. If the parties are unable to agree on costs, I will accept further written submissions from them not to exceed 7 pages in length.

JUDGMENT

THIS COURT'S JUDGMENT is that application is dismissed with costs payable to Apotex.

"R.L. Barnes"

Judge

FEDERAL COURT

SOLICITORS OF RECORD

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APPEARANCES:

Neil Belmore Marian Wolanski	FOR THE APPLICANTS
Andrew Brodkin Dino Clarizio Sandon Shogilev	FOR THE RESPONDENT APOTEX INC. CANADA INC.

SOLICITORS OF RECORD:

Belmore Neidrauer LLP Toronto, ON	FOR THE APPLICANTS
Goodmans LLP Toronto, ON	FOR THE RESPONDENT APOTEX INC. CANADA INC.
Myles J. Kirvan Deputy Attorney General of Canada Toronto, ON	FOR THE RESPONDENT THE MINISTER OF HEALTH