Federal Court  Cour fédérale

Date: 20140825

Docket: T-1667-12

Citation: 2014 FC 791

BETWEEN:

ALCON CANADA INC. AND
ALCON RESEARCH, LTD.

Applicants

and

APOTEX INC. AND
THE MINISTER OF HEALTH

Respondents

PUBLIC REASONS FOR JUDGMENT
(Confidential Reasons for Judgment issued August 11, 2014)

TABLE OF CONTENTS

Page

KANE J.

I. OVERVIEW

[1] This application, under the provisions of the *Patented Medicines (Notice of Compliance) Regulations*, SOR/93-133, as amended [*NOC Regulations*], seeks to prohibit the Minister of Health from issuing a Notice of Compliance [NOC] to Apotex in respect of its generic product (Apo-Travoprost Z, or the Apotex product) until the expiry of Canadian Letters Patent No 2,606,370 (the '370) on September 20, 2027.

[2] Apotex submits that the NOC should be issued because the claims of the Patent at issue are invalid.

[3] For the reasons that follow, I find that the allegations with respect to the invalidity of the claims at issue for obviousness are justified and the allegations with respect to invalidity for lack of utility are not justified.

[4] The application is dismissed with costs to the respondent.

II. INTRODUCTION

[5] The Patent at issue in this proceeding relates to Alcon's product, an ophthalmic solution typically used for the treatment of glaucoma.

[6] Glaucoma is a disease of the eye resulting in a progressive loss of vision due to increased intraocular pressure ["IOP"], which is the pressure within the aqueous humour of the eye.

Reducing IOP is the only way known to treat glaucoma. Such treatment is ongoing or "chronic" and requires the patient to take medication daily to maintain the IOP at a reduced level.

[7] Alcon notes that prostaglandin analogues, such as latanoprost and travoprost, are effective in lowering IOP and have become "mainstays" of treatment. Alcon further notes that travoprost is the active ingredient in Alcon's TRAVATAN® and TRAVATAN Z® products, which are administered topically to the surface of the eye using a small, multi-dose bottle that contains travoprost in solution.

[8] Such multi-dose topical ophthalmic solutions require preservatives to avoid microbial contamination. Contamination may result from repeated exposure to air, bodily fluids and tissues. Single-dose products do not require preservatives because they are used only once.

[9] The '370 Patent at issue claims formulations of travoprost, an anti-glaucoma drug, with a non-conventional preservative system to permit multi-use application.

[10] Apotex now wishes to market its own product, Apo-Travoprost Z, which is also a multi-dose ophthalmic solution containing travoprost with a non-conventional preservative system. Apotex requires a NOC in order to do so.

III. THE PARTIES

[11] The applicant, Alcon, is a "first person" as described in the *NOC Regulations*. It has listed the '370 Patent in accordance with the Regulations. Alcon obtained a Notice of

Compliance [NOC] to sell its multi-dose ophthalmic formulation preserved against microbial contamination, Travatan Z.

[12] The respondent, Apotex, is a "second person" as described in the *NOC Regulations*. In order to sell its generic product, Apo-Travoprost Z, it must obtain a NOC from the Minister of Health.

[13] In accordance with the *NOC Regulations*, Apotex served Alcon with a Notice of Allegation [NOA] dated July 25, 2012. In its NOA, Apotex alleges that Claims 10 and 13 of the '370 Patent are invalid on several grounds, as noted below, but now pursues only the allegations of obviousness and lack of utility. Apotex also alleges that it does not infringe any valid claim in making, constructing, using or selling its product.

[14] The Minister of Health, who has various responsibilities under the *NOC Regulations*, including the issuance of a NOC to a "second person" such as Apotex, took no active role in these proceedings.

IV. THE '370 PATENT GENERALLY

[15] Canadian Letters Patent No 2,606,370 were applied for by an application deemed to be filed with the Canadian Patent Office on September 20, 2007. The new *Patent Act*, RSC 1985 c P-4, governs this Patent, as it was applied for after October 1, 1989.

[16] The application was filed under the provisions of the Patent Cooperation Treaty [PCT] and claims priority from a first application filed in the United States Patent Office on September 21, 2006. This is the date upon which the issue of obviousness will be determined.

[17] The date of filing in Canada, September 20, 2007 is the date upon which the issue of utility (demonstrated or soundly predicted) will be determined.

[18] The publication date, i.e., the date at which the Patent was open to the public for inspection, was March 21, 2008. This is the relevant date for the purposes of the construction of the claims.

[19] The ‘370 Patent lists the inventors as Bhagwati P Kabra, Masood A Chowhan, L Wayne Schneider and Wesley Wehsin Han, all of the United States. Only Dr Kabra provided evidence in these proceedings.

[20] The ‘370 Patent was issued to Alcon Laboratories Inc, US.

[21] The term of the ‘370 Patent, unless declared as invalid, will expire 20 years from the date of the filing of the application in Canada, which is September 20, 2027.

[22] There are 35 claims in the ‘370 Patent; however, only Claims 10 and 13 are at issue in this proceeding. The construction of the claims and the inventive concept of the Patent are addressed below.

V. THE EVIDENCE

[23] The evidence was provided in the form of affidavits and transcripts of the cross-examination of the experts along with their exhibits. All experts were cross-examined. Each party also submitted the affidavits of law clerks to place documents on the record and attest to facts.

[24] The evidence on the record includes the following:

A. *For the applicant Alcon:*

(1) Kingsley Koo

[25] Kingsley Koo is a law clerk at Alcon's solicitor's office. His affidavit attaches a variety of documents, such as the '370 Patent, Apotex's Notice of Allegation, and Apotex's prior art references.

(2) Dr Bhagwati Kabra

[26] Dr Kabra is one of the inventors of the '370 Patent and describes Alcon's work leading to TRAVATAN Z and the '370 Patent. Dr Bhagwati Kabra holds an MSc and PhD in Chemical Engineering. He has been employed by Alcon and its predecessors since 1993.

(3) Dr Thorsteinn Loftsson

[27] Dr Loftsson is a Professor of Physical Pharmacy in the Faculty of Pharmaceutical Sciences at the University of Iceland. Dr Loftsson holds a MSc and PhD in Pharmaceutical

Chemistry, as well as a MSc in Pharmacy. In addition to teaching and research, he is a Director of a small pharmaceutical company and Board Member of another. He is a member of several professional societies, the author of more than 270 publications, and he has delivered more than 100 invited lectures. He describes his expertise in the formulation of multi-use ophthalmic solutions. He was asked by Alcon to, among other things, discuss the skills of the person skilled in the art, review the scientific background and common general knowledge related to self-preserved ophthalmic solutions, review the '370, identify the inventive concept of Claims 10 and 13, identify the utility of the Patent and respond to Apotex's allegations relating to anticipation, obviousness and inutility.

B. *For the respondent Apotex*:

(1) Lisa Ebdon

[28] Lisa Ebdon is a law clerk at Apotex's solicitor's office. Her affidavit attaches a variety of documents, including Apotex's Notice of Allegation, the prior art references, and a copy of the '370 Patent.

(2) Christopher Butler

[29] Christopher Butler is the Office Manager at the Internet Archive, which operates the Wayback Machine, a database that provides access to archived versions of the Internet. Mr Butler attaches documents about SYSTANE products obtained using the Wayback Machine.

(3) Lisa Lines

[30] Lisa Lines is a medical writer and PhD candidate in Health Services Research at the University of Massachusetts Medical School. Ms Lines attended and reported on the Association for Research in Vision and Ophthalmology [ARVO] 2006 annual meeting, including Alcon's tear replacement product SYSTANE® FREE.

(4) Dr John Kent

[31] Dr Kent earned a PhD in Pharmaceutics in 1969 and was employed by several pharmaceutical companies from 1965 until 2008. He has been a consultant to the pharmaceutical industry since 2008. Dr Kent worked at Allergan between 1990 and 2002. He describes his expertise in ophthalmic formulation development and notes that he developed more than 10 ophthalmic pharmaceuticals that were commercially launched. He was asked, among other things, to describe the person skilled in the art, to provide opinions on the scope and meaning of the claims, the inventive concept of the claims, whether certain prior art documents were available to the public as of September 21, 2006, whether the prior art discloses the subject matter of the claims, the differences if any between the state of the art and the inventive concept of the claims (i.e. whether the Patent was obvious), the utility of the Patent and whether that utility had been demonstrated or soundly predicted. In addition, Dr Kent reviewed the affidavits of Dr Kabra and Dr Loftsson and provided comments.

(5) Dr Michael Miller

[32] Dr Miller holds a PhD in Microbiology and Biochemistry. Dr Miller worked at Bausch & Lomb in various capacities between 1991 and 2002 and at Eli Lilly from 2003 to 2009 and is

currently President of Microbiology Consultants, LLC. He describes his expertise in the field of ophthalmic compositions and antimicrobial preservation of such compositions including self-preserved ophthalmic compositions. He was asked by Apotex, among other things, to provide a scientific primer, and to provide his opinion on the state of the art as of September 21, 2006, the inventive concept of the claims, the differences between the inventive concept and the state of the art and whether those differences would be self-evident. He was also asked to review and comment on the affidavits of Dr Kabra and Dr Loftsson.

VI. ISSUES

[33] The overall issue is whether to grant an Order prohibiting the Minister of Health from granting a Notice of Compliance to Apotex for its generic product (Apo-Travoprost Z) until the expiry of the '370 Patent. This determination depends upon whether the allegations raised by Apotex as to the invalidity of particular claims of the '370 Patent are justified.

[34] Apotex alleges that the claims at issue are invalid on the basis of obviousness and lack of demonstrated or soundly predicted utility. To provide the relevant context for the analysis of the allegations, the assessment of the evidence and my findings, a brief overview of the positions of Alcon and Apotex follows.

A. *Alcon's overall position*

[35] Alcon notes that the Patent relates to a self preserved multi-dose formulation, using multi-functional components to avoid microbial activity. The invention does not use benzalkonium chloride [BAK or BAC], which had been known to cause side effects. Alcon

submits that there are at least four inventive concepts for the claims at issue and that the invention was not obvious. Alcon further submits that although the inventive concepts are several and specific, the promised utility is simply to provide a formulation that passes USP preservative efficacy testing [PET] and is useful or provides another choice. Alcon submits that this utility was soundly predicted.

[36] Alcon disputes that the promised utility is also to minimize or eliminate toxicological effects. However, Alcon submits, that if this were the promised utility, it was also soundly predicted.

[37] Alcon disputes Apotex's new or revised assertion of promised utility; that the promised utility is to provide an "acceptable" pharmaceutical composition or formulation where "acceptable" means without the possibility of particulate matter forming. Alcon notes that this was not asserted as the basis for the allegation of lack of utility by Apotex in its NOA, and as such, this new basis for the allegation cannot be considered.

B. *Apotex's overall position*

[38] Apotex argues that Alcon seeks to read the inventive concept of the Patent in one way to support its inventiveness and to read it another way to support its utility, as simply being useful.

[39] Apotex submits that the invention was obvious; Alcon sought to replace BAK with another preservative system to avoid the side effects and the prior art taught how to do so. In particular, Alcon need not have looked any farther than its own preservative system used in

Systane Free or a system similar to that of Systane Free. Apotex further argues that the prior art and common general knowledge would lead a POSITA to this invention.

[40] Apotex now also submits, as a new or revised assertion, that the promised utility of the multi-dose formulation is to provide an "acceptable" formulation, meaning that particulate matter will not occur. Apotex's original assertion of the promised utility is the use of the components of the invention in an aqueous ophthalmic solution so as to eliminate the need for BAK and to minimize or eliminate the toxicological effects. Apotex submits that neither the original nor the revised promised utility was soundly predicted.

[41] Apotex submits that Alcon cannot rely on the resolution of the particulate matter problem as part of the inventive concept yet deny that it is part of the promised utility.

[42] Apotex also argues that it cannot be precluded from responding to this aspect of the inventive concept despite that it did not raise this as the promised utility in the NOA.

[43] The overview of the parties' positions understates the complexity of the arguments advanced in this application. The position of both parties appears to have evolved and both have raised alternative arguments and have responded with alternatives to the alternatives, further complicating the determination of the key issues, the allegations of obviousness and lack of demonstrated and soundly predicted utility. Although some of the issues raised by the parties are not determinative given my findings with respect to the scope of the NOA, construction of the

claims, determination of the inventive concept, and determination of the promised utility, all of the arguments of the parties and the voluminous evidence have been carefully considered.

VII. THE NOTICE OF ALLEGATION [NOA]

[44] In the Notice of Allegation, Apotex broadly alleges that all claims of the '370 are invalid on the basis of one or more of the following grounds; lack of novelty/anticipation, obviousness, lack of demonstrated utility, no sound prediction of utility and failure of utility.

[45] With respect to the inventive concept, Apotex alleges at page 28:

> […] there is no invention in the claims of the '370 Patent, and therefore there is no inventive concept in any of the claims of the '370 Patent.
>
> Alternatively, Apotex alleges that, if anything, the inventive concept of the claims of the '370 Patent is the use of the recited components (*e.g.* zinc ions, borate/polyol complex, etc.) at their respective concentrations in the claimed aqueous ophthalmic solutions so as to eliminate the need for the preservative BAK, thus avoiding deleterious effects on the cornea.

[46] With respect to the allegations of obviousness, Apotex set out the prior art relating to: zinc ions and preservatives in ophthalmic compositions including the prior art listed in the '370; borate/polyol complexes; travoprost; polyoxyl 40 hydrogenated castor oil; and, osmolality.

[47] At page 33, with respect to borate/polyol complexes, Apotex notes:

> Further, an Alcon tear replacement product, SYSTANE® Free LIQUID GEL Lubricant Eye Drops, which was sold between 2005 and 2006 in the United States, incorporated a borate/polyol complex composed of boric acid, sorbitol and propylene glycol. This product was also well known to the person skilled in the art.

[48] At page 69-70, Apotex notes:

> Further, as of September 2006, the person skilled in the art would have understood the zinc ion/borate/polyol preservative system to be a viable alternative to BAK in ophthalmic compositions/solutions. The person skilled in the art would have been aware of Alcon's own use of such a preservative system in their SYSTANE® artificial tears product. Therefore, the person skilled in the art, as of September 2006, would have identified the use of a zinc ion/borate/polyol preservative system as a predictable solution addressing the use of BAK in an aqueous ophthalmic solution.

[49] The NOA includes two publications by McCarthy: McCarthy 1985 (*Metal Ions and Microbial Inhibitors*) and McCarthy 1989 (*The Effect of Zinc Ions on Antimicrobial Activity of Selected Preservatives*) in the list of prior art with respect to zinc ions as preservatives at page 29.

[50] With respect to the promised utility, Apotex alleges that the invention is the use of zinc ions in combination with borate and optionally polyols as a preservative system in multi-dose ophthalmic compositions. Noting that the '370 indicates that BAK results in potential harmful effects on the cornea and that it should be avoided, Apotex concludes, "The preservative systems of the claimed ophthalmic compositions/solutions exhibit antimicrobial activity ("self preserved") with concomitant minimization or elimination of toxicological effects (harmful effects on the cornea). Hereafter, this will be referred to as the 'Promised Utility'".

[51] Apotex alleges that it was well known that the treatment of glaucoma requires control of IOP and long term application of the drug to the eye and a POSITA would understand that because the intended use was to control IOP, compositions or solutions that are promised to

minimize or eliminate toxicological effects would require evaluation, however, none had been done. Apotex, therefore, alleges that Alcon has not demonstrated or soundly predicted utility.

[52] The NOA notes that several claims are irrelevant, but sets out allegations of obviousness and lack of demonstrated or soundly predicted utility of all claims, as noted above.

[53] The claims at issue in the present application are Claims 10 and 13.

A. *Alcon's position on the NOA*

[54] Alcon acknowledges that Apotex's Notice of Allegation alleges invalidity of Claims 10 and 13 on the following grounds: the claimed invention is obvious in view of the prior art and certain Alcon products; and the '370 Patent promises "ophthalmic compositions/solutions [that] exhibit antimicrobial activity ("self-preserved") with concomitant minimization or elimination of toxicological effects (harmful effects on the cornea)" and that the '370 Patent fails to demonstrate or soundly predict that promised utility.

[55] Alcon disputes both allegations.

[56] Alcon also notes that other issues raised in the NOA have not been pursued: for example, that other claims of the '370 Patent are anticipated and/or irrelevant and that the claims are broader than the invention. Alcon notes that although these are not pursued, it does not accept that the claims are anticipated.

[57] Alcon notes that the NOA serves two purposes; it allows the first person to know the case to meet and it limits the issues. Alcon submits that Apotex has exceeded the limits by raising new issues that were not in the NOA.

[58] Alcon submits that the following issues were not raised in the NOA: that the prior art, specifically the McCarthy publications, set out limits on anionic species; the particulars of the Systane Free formulation; and, the allegation of lack of demonstrated or soundly predicted utility for the revised or new promised utility of an acceptable formulation (based on Apotex's premise that particulate matter is not acceptable for ophthalmic solutions).

[59] Alcon argues that there is a distinction between responding to evidence that arises regarding the allegations set out in the NOA and advancing new allegations or further bases of invalidity for those allegations. Alcon argues that responding to the evidence of an expert, in this case, Dr Loftsson, does not permit Apotex to raise new grounds of invalidity or new bases for the allegations set out in the NOA.

[60] Alcon submits that Apotex cannot now argue that there is no sound prediction of acceptable ophthalmic solutions due to the particulate problem because this was not set out in its NOA nor is there such a promised utility.

B. *Apotex's position on the NOA*

[61] Apotex submits that the NOA must provide adequate notice to permit the first person, Alcon, to decide whether to bring its Notice of Application. In this case, Alcon had sufficient notice and did so. Alcon's conduct in this litigation showed that they knew the case to meet.

[62] Apotex notes that Alcon did not seek any further clarification from Apotex despite the invitation in the NOA to do so. In addition, Alcon did not submit an affidavit to indicate how it had been prejudiced by the alleged omissions. Moreover, Apotex argues that it cannot be denied an opportunity to address the issues that Alcon raised in support of the validity of the claims at issue that could not have been anticipated and which were raised in response to the evidence of Alcon's only expert witness, Dr Loftsson.

[63] Apotex argues that Alcon ignored a key piece of the prior art relevant to the allegations of obviousness: that relating to its own product, Systane Free. Systane Free was a multi-dose ophthalmic composition that used zinc ions with a borate/polyol complex to avoid the need for a traditional preservative. However, Alcon's own expert did not consider Systane Free in his review of the prior art or in his opinion on obviousness and it appears that he was instructed to ignore Systane Free.

[64] Apotex notes that its NOA clearly referred to Systane Free to support its allegations of obviousness and directed the reader to the details which could be found in another document referred to in a footnote. Apotex subsequently led evidence to establish that Systane Free was marketed before 2006 for the purpose of correcting the misinformation of Alcon's expert, Dr Loftsson, that the details of Systane Free were only available after 2006, the relevant date for the obviousness assessment.

[65] With respect to the composition details of Systane Free, which Alcon argues are not relevant and should not be considered because they were not set out in the NOA, Apotex notes that the footnote in the NOA directs Alcon to one of its own documents.

[66] The NOA also advised Alcon to make inquiries or seek clarification of the NOA and it did not. Alcon requested other documents but did not request the document regarding Systane Free.

[67] Apotex submits that Alcon cannot succeed in its argument that the NOA was deficient in not providing the formulation details of Systane Free given these circumstances and given that it was Alcon's own product of which they had all the details.

[68] With respect to the reliance on and reference to the prior art publications by McCarthy, Apotex notes that it referred to the publications in its NOA. Apotex submits that it relies on the content of the McCarthy publications to counter Dr Loftsson's evidence that nothing in the prior art indicated that the anionic species should be kept below 15mM. Apotex notes that McCarthy did just that.

[69] Apotex submits that Alcon's position that there are at least four inventive concepts, including overcoming the formation of particulates, is based on the evidence of Dr Loftsson, which Alcon later adopted.

[70] Apotex argues that a second person must be permitted to respond to issues raised by a first person that it could not have anticipated, otherwise there would be an incentive for the first person to raise new arguments to support the validity of a patent and take the second person off guard, knowing the second person would be prevented from responding. Apotex submits that it has a right to respond to any issue or position raised by Alcon.

[71] Apotex further submits that Alcon asserts that the NOA is deficient (i.e., that Apotex did not allege that the promised utility includes avoiding particulate matter) only to foreclose Apotex's utility challenge. Apotex argues that the evidence revealed that there was no sound prediction that compositions falling within the asserted claims would not form particulate matter. So, to avoid the claim being invalid for not meeting the promised utility of an acceptable formulation, Alcon seeks to prevent Apotex from raising the revised promise of utility.

C. *Jurisprudence and Principles Regarding a Notice of Allegation*

[72] Apotex relies on the jurisprudence which has held that a second person is not required to anticipate every theory of possible infringement, for example, *AstraZeneca AB v Apotex Inc*, 2005 FCA 183, [2005] FCJ No 842 [*Omeprazole*] at para 11. Similarly in *Novopharm v Pfizer*, 2005 FCA 270, [2005] FCJ No 1318 at para 16, the Court of Appeal addressed the issue of the adequacy of the NOA, stating:

> [16] […] Whether Novopharm's NOA was adequate depends on whether it provided Pfizer with a sufficient understanding of the case it had to meet (supra at paragraph 4). The legal test of adequacy does not require Novopharm to anticipate all possible grounds of infringement, including Pfizer's speculative theory that the dihydrate could be used in the process of manufacturing Novopharm's bulk monohydrate. As noted by Evans J.A. in

> *AstraZeneca AB v. Apotex Inc.* 2005 FCA 183, [2005] F.C.J. No. 842 (QL) at paragraph 11:
>
> > A second person [the generic] should not be required to anticipate every theory of possible infringement, however speculative, in the detailed statement supporting its allegations.

[73] In *Novopharm*, the Court of Appeal noted that Pfizer was not left to guess at the real grounds for the allegation and also noted that Pfizer had raised the issue by filing evidence from its expert.

[74] While the second person cannot be expected to anticipate every possible theory, the jurisprudence has established that the requirements of the NOA must be observed.

[75] In *Bayer Inc v Cobalt Pharmaceuticals Co*, 2013 FC 1061, [2013] FCJ No 1152 [*Bayer*] at paras 34-36, Justice Hughes emphasized the requirement for the second person to raise all the facts and legal arguments it will rely upon in its NOA and that it cannot raise new arguments, new allegations, new facts or new prior art documents that are not set out in the NOA. Justice Hughes acknowledged that this approach may seem "draconian" but that "it is equally draconian for the first person who decides to institute proceedings to face shifting allegations and facts" and added, "As matters stand now, the Court must reject arguments based on facts or documents not set out in the Notice of Allegation nor can the Court address new allegations".

[76] This principle has been applied to issues that arose after the NOA had been served and which the second person would not have been aware.

[77] In *Pfizer Canada Inc v Mylan Pharmaceuticals ULC*, 2011 FC 547, [2011] FCJ No 686 at paras 197-198, Justice Hughes addressed Mylan's argument that some of the testing data in the Patent at issue was inaccurate. The NOA did not raise the issue whether the testing and data set out in the patent accurately presented what was done at Eisai. Justice Hughes held that the Court could not consider such matters noting that "The issue in these NOC proceedings must be determined on the basis of what is set out in the Notice of Allegation."

[78] The Court of Appeal agreed, noting that Justice Hughes was aware that Mylan could not have known that the data was inaccurate until after the NOA was served and could not, therefore, have included such an allegation in its NOA (*Pfizer Canada Inc v Mylan Pharmaceuticals ULC*, 2012 FCA 103, [2012] FCJ No 386). However, the NOA did not include the allegation that the work done by the applicant Eisai was not fully and accurately set out in the Patent. The Court stated at para 29:

> 29 It is well established that a Notice of Allegation frames the proceeding under the *NOC Regulations*, and that any allegation which is not included in that notice cannot be addressed in the proceeding: […] The special proceedings under the *NOC Regulations* are meant to be summary. There is no discovery phase, and the proceedings are thus necessarily limited to the legal grounds and specific factual allegations set out in a Notice of Allegation, which cannot be subsequently amended. This is a well understood feature of a proceeding under the *NOC Regulations*.

[79] The Court of Appeal also noted at para 31 that the scope of allegations in an NOA must be determined in each case with a view to the language of the NOA and the evidence and that each case is highly fact-specific.

[80] The lack of an affidavit has also been found to be a relevant factor in the determination whether the first person has been prejudiced by new issues that were not raised in the NOA.

[81] In *Aventis Pharma Inc v Apotex Inc*, 2006 FCA 64, [2006] FCJ No 208 at para 15, the Court of Appeal found that the applications judge had considered the sufficiency of the NOA as it related to the issue of sound prediction, applied the relevant law and determined that the NOA had put Aventis on notice of the sound prediction argument. The Court of Appeal confirmed that the applications judge properly considered the lack of an affidavit on the part of Aventis "to be telling" in her consideration of the sufficiency of the NOA.

[82] The Court of Appeal made similar comments in *Omeprazole*, above, at para 13 regarding the lack of an affidavit on the part of AstraZeneca to describe how it had not been able to decide whether to challenge Apotex's NOA because of the lack of specificity in the NOA.

D. *The scope of the NOA*

[83] The scope of the allegations must be determined in each case based on the language of the Notice of Allegation at issue as well as the evidence submitted.

[84] In the present case, the Notice of Allegation raised allegations of invalidity based on obviousness and lack of demonstrated and soundly predicted utility based on the promised utility as Apotex originally alleged, i.e., the use of zinc ions in combination with borate and, optionally, polyols as a preservative system in multi-dose ophthalmic compositions with concomitant minimization or elimination of toxicological effects (harmful effects on the cornea). The NOA

did not allege lack of soundly predicted utility of an acceptable ophthalmic composition, which Apotex now asserts.

[85] The case law is clear that the generic or second person cannot craft new arguments, or raise new allegations, new facts or new prior art documents which were not set out in the Notice of Allegation.

[86] Apotex does not rely on new prior art as it was all set out in the NOA, including the references to Systane Free and McCarthy.

[87] Systane Free was set out specifically in the NOA and this was sufficient notice to Alcon that it would be relied on as part of the prior art. Alcon was directed to the details of the product, and given that it was an Alcon product, Alcon cannot credibly argue that the footnote reference was not sufficient.

[88] With respect to the reference to McCarthy, both publications were referred to in the NOA, albeit not with details about why the publications would be relied on.

[89] Nor does Apotex rely on new allegations; the allegations remain obviousness and lack of demonstrated or soundly predicted utility. However, Apotex raises new and different underlying facts to support the allegations of invalidity by asserting the promised utility of an acceptable formulation, meaning one without particulate matter.

[90] I am not persuaded by Apotex's argument that, because Alcon did not identify the resolution of the particulate problem as one of the inventive concepts in its Notice of Application, Apotex was not aware that the inventive concept was a live issue and it must now be permitted to assert a new basis for its allegation of lack of demonstrated or soundly predicted utility that is more closely aligned with this proposed aspect of the inventive concept. It is not unusual or surprising that Alcon would assert its view of the inventive concept or would dispute the inventive concept asserted by Apotex.

[91] The issue of the revised promise of utility of an acceptable formulation is a new basis for the allegation of lack of demonstrated or soundly predicted utility. Apotex now seems to put more reliance on this promise than its original assertion of the promised utility. However, Apotex also argues that resolving the particulate problem is not part of the inventive concept. Apotex alternatively argues that, if the Court finds that it is, the promised utility must align with this aspect of the inventive concept.

[92] The jurisprudence is clear; the proceedings are limited to the legal grounds and specific factual allegations set out in a Notice of Allegation.

[93] I have considered whether allowing Apotex to raise this new basis for the allegation of lack of soundly predicted utility, although not specifically forecasted and not set out in its NOA, causes Alcon to "face shifting allegations and facts".

[94] Apotex has clearly raised a new factual basis or argument that was not in the NOA to buttress or refine its allegations of lack of utility. On the other hand, Alcon did not submit an affidavit to provide evidence of how it was prejudiced in responding to the new argument. Alcon brought this application and raised many arguments in response to Apotex as well as new issues that could not have been anticipated prior to Dr Loftsson's evidence.

[95] With respect to the new assertion regarding promised utility, I must agree with Justice Hughes in *Bayer* above, "As matters stand now, the Court must reject arguments based on facts or documents not set out in the Notice of Allegation nor can the Court address new allegations." The Court will not address the allegation of lack of utility based on the promise of an "acceptable" formulation.

[96] However, much of Apotex's detailed arguments regarding the particulate issue is in response to Alcon's argument that this is part of the inventive concept. Therefore, Apotex may respond to Alcon's position on the inventive concept but it cannot assert a revised promise of an "acceptable' (i.e. no particulate matter) formulation as the basis for its allegations of invalidity based on lack of utility.

[97] Despite my conclusion that the revised assertion of the promise of utility is beyond the scope of the NOA, it has no bearing on the outcome because the inventive concept does not include finding the solution to the particulate problem.

VIII. BURDEN

[98] Apotex argues that it has put the issues of lack of utility (demonstrated and soundly predicted) and obviousness into play and Alcon now bears the burden of establishing the allegations are not justified. Apotex argues that Alcon has not met this burden on a balance of probabilities and that in the event the Court finds the evidence is evenly balanced, it must find that Alcon has not met its burden.

[99] The jurisprudence has settled who bears the burden of proof of the allegations.

[100] As I noted in T-1666-12 (*Alcon v Apotex*), which was heard immediately before this application and which deals with a different patent, as a starting point, where the validity of a patent is at issue, the patent will be presumed to be valid. However, where a generic manufacturer (a second person), in this case Apotex, raises allegations of invalidity and adduces some evidence capable of establishing the invalidity of the patent, the generic is said to put the issue "into play". The burden then moves to the brand or applicant (first person), in this case, Alcon, to establish on a balance of probabilities that all of the allegations of invalidity are not justified: see *Lundbeck Canada Inc v Ratiopharm Inc*, 2009 FC 1102, [2009] FCJ 1466; *Abbott Laboratories v Canada (Minister of Health)*, 2007 FCA 153, [2007] FCJ No 543 at paras 9-10; *Pfizer v Canada (Minister of Health)*, 2007 FCA 209, [2007] FCJ No 767 at para 109 (FCA); *Allergan Inc v Canada (Minister of Health)*, 2012 FC 767 [*Allergan*] at para 42 affirmed in the result 2012 FCA 308; *Pfizer Canada Inc v Pharmascience Inc*, 2013 FC 120, [2013] FCJ 111 at paras 24-27; *Bayer v Cobalt*, 2013 FC 573.

[101] Justice O'Reilly set out the approach to be followed with respect to the burden of proof in *Pfizer Canada Inc v Apotex Inc*, 2007 FC 26, [2007] FCJ No 36 (aff'd 2007 FCA 195, leave to appeal refused 32169 (November 1, 2007)) at paragraphs 9 and 12, characterizing the burden on the respondent as "an 'evidential burden'-- a burden merely to adduce evidence of invalidity". The respondent must adduce evidence to give its allegations an air of reality, and if it does so, it has put the issues "into play" and the presumption of validity no longer applies. The applicant must then discharge its legal burden of proof to the satisfaction of the court on a balance of probabilities.

[102] In the present case, if the generic, Apotex, does not adduce any evidence with respect to a ground of invalidity alleged, then the presumption is not rebutted. Similarly, if Apotex adduces some evidence but that evidence is insufficient to meet its evidential burden or does not have an "air of reality", the issues would not be put into play and Alcon would continue to rely on the presumption of validity to obtain its prohibition order.

[103] However, if Apotex presents sufficient evidence to give its allegations an air of reality, then the presumption of validity is rebutted and the issue then becomes whether Alcon has established that Apotex's allegations of invalidity are not justified.

[104] In *Allergan* at para 42, Justice Hughes set out the same principles noted above which he had set out in his earlier decision in *GlaxoSmithKline Inc v Pharmascience Inc*, 2011 FC 239, [2011] FCJ No 287 at paras 43 and 44, where he noted six steps in the assessment of the

allegations and the applicable burden of proof. Justice Hughes indicated, following step 5, which is the weighing of the evidence on a balance of probabilities:

> *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.*

[105] In *Biovail Corp v Canada (Minister of Health)*, 2010 FC 46, [2010] FCJ No 46 at paras 40-41 and 107, Justice Kelen applied the six step approach, set out his analysis of the law to the evidence, and found that the evidence was evenly balanced at the obvious to try step, noting, at para 107:

> […] Because the applicant has the onus of proof and because the Court has concluded that the evidence on this important "obvious to try" test criteria is evenly balanced, the applicant has not satisfied its onus to prove, on a balance of probabilities, that the allegation in this regard was unjustified. For this reason, the Court must dismiss this application.

[106] In the present case, Apotex raised allegations in its NOA and led sufficient evidence as to the invalidity of the Patent on the basis of obviousness and lack of demonstrated or soundly predicted utility to put those broad allegations and issues into play. As noted above, the allegation of lack of utility based on the revised assertion of promised utility is beyond the scope of the NOA. Alcon now bears the burden of establishing on a balance of probabilities that the allegations are not justified.

IX. PERSON SKILLED IN THE ART

[107] There is no dispute about the qualifications of the person of skill in the art [POSITA], also referred to as the skilled person.

[108] Dr. Loftsson proposes, at para 21 of his affidavit, that the skilled person "is a pharmaceutical formulator or a person with an undergraduate degree in, for example, organic chemistry, biochemistry, medicinal chemistry or chemical engineering" and "would likely also hold a graduate degree in pharmaceutical sciences or pharmaceutics, with 3 to 5 years of experience in the formulation of ophthalmic products, including solutions".

[109] Dr Millar states, at para 46 of his affidavit, that the skilled person would have a PhD in microbiology or chemistry (or a related field) with at least a few years of experience in the development of ophthalmic formulations or would have a BSc or MSc in microbiology or chemistry (or a related field) with significant experience (five years or more) in the development of ophthalmic formulations. He added that the skilled person would work as part of a multi-disciplinary team and draw on his own skills and the specialized skills of others to solve a formulation problem.

[110] At para 45 of his affidavit, Dr Kent expresses the view that the skilled person would be a team of persons that includes pharmaceutical scientists/formulators and microbiologists who would have knowledge of how to formulate ophthalmic compositions, in particular self-preserved multi-dose ophthalmic solutions. Representative individuals on the team would have a PhD in chemistry, pharmacy, microbiology or a related field with limited experience or a BSc or MSc with more practical experience (five or more years) in the formulation of such preserved ophthalmic formulations.

[111] The POSITA for the ‘370 can, therefore, be described as:

- The team of person that includes pharmaceutical scientists / formulators and microbiologists. These persons have knowledge of how to formulate ophthalmic compositions, in particular, preserved multi dose ophthalmic solutions for topical application. Representative individuals on the team would have a Ph.D. in chemistry, pharmacy, microbiology or a related field with limited experience (up to 3 years) or a B.Sc. or M.Sc. with more practical experience (5 or more years) in the formulation of such preserved ophthalmic formulations.

X. THE ‘370 PATENT IN DETAIL

[112] The title of Canadian Patent 2,606,370 is *self-preserved aqueous pharmaceutical compositions*.

[113] At page 1, the *Background of the Invention* provides:

> *The present invention is directed to self-preserved pharmaceutical compositions. More specifically, the invention is directed to the provision of aqueous, multi-dose pharmaceutical compositions that have been formulated so as to have sufficient antimicrobial activity to satisfy the preservation efficacy requirements of the United States Pharmacopeia (“USP”) and analogous guidelines in other countries, without requiring a conventional antimicrobial preservative, such as benzalkonium chloride, polyquaternium-1, hydrogen peroxide (e.g., sodium perborate), or chorine-containing agents. The ability to achieve self-preservation is based on a unique combination of formulation components and criteria.*

[114] The Patent then explains that many pharmaceutical compositions are required to be sterile and that procedures to do so are well known to POSITAs. It notes that the sterility of multi-dose products may be compromised due to their exposure to the atmosphere and other sources of

contaminants. Some means of preventing contamination is necessary; either a chemical agent or a packaging system.

[115] The Patent then notes that in order to minimize the potential for harmful effects on the cornea, it is preferable to use anti-microbial preservatives that are relatively non-toxic at the lowest possible concentrations (described as "the minimum amounts required in order to perform their anti-microbial functions").

[116] The Patent notes that the balance between the antimicrobial efficacy and the toxicological effects of these preservatives is sometimes difficult and that the lower concentrations may be insufficient to achieve the required level of antimicrobial preservation.

[117] At page 3, the Patent states the need to address this challenge as follows:

> *Thus, there is a need for a means of enhancing the activity of anti-microbial agents so that very low concentrations of the agents can be utilized without increasing the potential for toxicological effects or subjecting patients to unacceptable risks of microbial contamination and resulting ophthalmic infections.*

[118] The Patent notes the approach of using multi-functional components to enhance the antimicrobial activity of ophthalmic compositions and identifies references in the art on the use of multifunctional components, including several US patents.

[119] The Patent states at page 3:

> *The use of zinc to enhance the antimicrobial activity of pharmaceutical compositions, including ophthalmic solutions, is well known. See, for example, the following articles and patent publications, as well as U.S. Patent No. 6,348,190 and JP 2003-104870, cited above (which refers to the art relating to multifunctional components.)*

[120] The Patent then sets out the references in the art regarding zinc, including:

> *McCarthy, "Metal Ions and Microbial Inhibitors", Cosmetic & Toiletries, 100:69-72 (Feb. 1985);*
>
> *Zeelie, et al., "The Effects of Selected Metal Salts on the Microbial Activities of Agents used in the Pharmaceutical and Related Industries", Metal Compounds in Environment and Life, 4:193-200 (1992);*

[121] The Patent also notes Zeelie, 1998 and McCarthy, 1980 and several US Patents.

[122] At page 4, the Patent indicates:

> *The present invention is directed to the provision of improved preservative systems containing zinc ions.*
>
> *The compositions of the present invention are multi-dose products that do not require a conventional antimicrobial preservative (e.g., benzalkonium chloride), and yet are preserved from microbial contamination. Such compositions have been referred to in the art as being "preservative free" (see, e.g., U.S. Patent No 5,597,559 issued to Olejnik, et al.). Compositions that are preserved from microbial contamination as a result of the inherent antimicrobial activity of one or more components of the compositions are also referred to in the art as being "self-preserved" (see, e.g., U.S. Patent No 6,492,361 issued to Muller, et al.).*

[123] The Patent directs the reader to the 1997 publication of Kabara et al regarding preservative free and self preserving pharmaceutical compositions.

[124] At pages 5-6, the Summary of the Invention states:

> *The present invention is directed to the self-preservation of aqueous ophthalmic compositions via the use of very low concentration of zinc ions. The present invention is based in part on the finding that in order to utilize low concentrations of zinc ions to self-preserve multi-dose ophthalmic compositions having ophthalmically acceptable pH and osmolality values, certain formulation parameters must be maintained. Specifically, the concentration of buffering anions utilized to maintain the pH within an ophthalmically acceptable range must be limited to an amount of 15 millimolar ("mM") or less in order to avoid interfering with the anti-microbial activity of the zinc ions.*
>
> *In addition, it has been determined that the antimicrobial activity of the zinc-containing compositions of the present invention can be further enhanced by the use of zinc ions in combination with borate or a borate/polyol complex, and that if such a combination is utilized, the use of propylene glycol is strongly preferred, so as to avoid ionic interactions between anionic species by other polyols (e.g., sorbitol) and the zinc cations.*
>
> *It has also been determined that the performance of the zinc-based preservative systems of the present invention is further enhanced by: (i) limiting the amount of multivalent metal cations other than zinc (e.g., calcium and magnesium) in the compositions of the present invention; and (ii) limiting the amount of ionized salts (e.g., sodium chloride and potassium chloride) in said compositions. As described in greater detail below, the compositions of the present invention are preferably free of or substantially free of both ionized salts and multivalent metal cations other than zinc.*
>
> *The self-preserved, multi-dose compositions of the present invention have several advantages over existing ophthalmic formulations that are either: (i) packaged as a "single dose" or "unit of use" product, so as to avoid the inclusion of any antimicrobial preservative (e.g., BION®TEARS Lubricant Eye Drops, which is marketed by Alcon Laboratories, Inc.), or (ii) preserved by means of a so-called "disappearing" preservatives, such as the chlorite-based system described in U.S. Patent Nos.*

> *5,424,078; 5,736,165; 6,024,954; and 5,858,346 (e.g., the artificial tears product "REFRESH™ Tears", which is marketed by Allergan), or the peroxide-containing system described in U.S. Patent Nos. 5,607,698; 5,683,993; 5,725,887; and 5,858,996 (e.g., the artificial tear product "GenTeal™ Tears", which is marketed by CIBA Vision).*
>
> *Unlike these existing products, the multi-dose ophthalmic compositions of the present invention are able to satisfy the USP preservative efficacy requirements, as well as analogous requirements in other countries, including the Japanese Pharmacopoeia ("JP") and European Pharmacopoeia ("EP") preservative efficacy standards, without employing any conventional antimicrobial preservatives, such as chlorite or hydrogen peroxide.*
>
> *The above-discussed findings regarding the zinc may be applied to enhance the antimicrobial activity of various types of pharmaceutical compositions. However, the present invention is particularly directed to the provision of aqueous ophthalmic solutions that are effective in preventing microbial contamination in the absence of conventional antimicrobial preservatives, such as benzalkonium chloride ("BAC"), polyquaternium-1, chlorite or hydrogen peroxide.*

[125] At pages 6a-6c various embodiments of the invention are described. The invention is indicated to provide "a use of travoprost in a composition or solution of the invention for control of intraocular pressure". A detailed description of the invention commences at page 6c and describes the preferred concentration of zinc ions, the preferred concentration of anionic species, the preference to not include multivalent buffering anions other than borate-polyol complexes, and other such preferred and non-preferred substances.

[126] At page 10, the Patent states:

> *The present invention is particularly directed to the provision of multi-dose, self-preserved ophthalmic compositions that have sufficient antimicrobial activity to allow the compositions to satisfy the USP preservative efficacy requirements , as well as other preservative efficacy standards for aqueous pharmaceutical compositions, without a conventional antimicrobial preservative.*

[127] At page 11, the preservative efficacy standards for multi-dose ophthalmic solutions in the US and other countries are set out in a chart.

[128] At pages 11-15 various optional substances, concentrations and therapeutic agents are described.

[129] At page 13, the Patent indicates that the invention is "particularly directed" to the use of the self preserved multi-dose ophthalmic compositions in connection with the treatment of certain conditions, and that the compositions are particularly useful in the field of artificial tears, ocular lubricants and other compositions used to treat dry eye as well as other conditions involving ocular inflammation or discomfort. Due to direct application to the eye, the Patent notes that the composition should be formulated to have a pH and tonicity compatible with the eye.

[130] The preferred pH range for compositions intended for direct application to the eye is noted to be "in the range of 4 to 9, preferably 5.5 to 8.5, and most preferably 5.5 to 8.0". Noting that a slightly alkaline pH increases the antimicrobial activity, the Patent states "The use of a pH in the range of 7.0 to 8.0 is therefore preferred".

[131] At page 14, the Patent notes that where cationic or anionic excipients are utilized adjustments may be required. It states, "For example, the nonionic surfactant polyoxyl 40 hydrogenated castor oil can be used for solubilization or stabilization of drugs, such as travoprost. However, it has been determined that 12-hydroxy stearic acid, an anionic compound that has been determined to be present as an impurity and potential degradation product of the excipient polyoxyl 40 hydrogenated castor oil, interacts with zinc and forms particles."

[132] The Patent then indicates at lines 28-31 that to avoid the particle formation in a composition containing these components the pH of the composition needs to be in the range of 5.0-6.0 and preferably 5.5-5.9, and directs the reader to Example Y.

[133] At pages 15-38 Examples A-Z and AA-DD describe the embodiments or aspects of the invention.

[134] The 35 Claims of the Patent are set out at pages 40-41.

[135] Only two claims, 10 and 13, are at issue in this application. As Claim 10 is dependent on Claims 1-9, which in turn are dependent in a cascading manner from Claim 1, it is also set out.

[136] *Claim 1* - A multi-dose, self-preserved ophthalmic composition, comprising zinc ions at a concentration of 0.04 to 0.4 mM, wherein the concentration of anionic species present in the composition is less than 15 mM.

[137] *Claim 10* - A composition according to any one of Claims 1-9, further containing travoprost as a therapeutically active agent.

[138] *Claim 13* - A topical ophthalmic solution comprising:

- 0.004 w/v % travoprost;
- polyoxyl 40 hydrogenated castor oil;
- a preservative system comprising (a) boric acid, (b) propylene glycol, (c) sorbitol, and (d) zinc chloride in a concentration of 0.04 to 0.4 mM;
- an amount of sodium hydroxide and / or hydrochloric acid to adjust the pH range of the solution to 5.5 to 5.9; and
- purified water;

wherein

- the solution is free of benzalkonium chloride or another antimicrobial preservative;
- the concentration of the anionic species present in the composition is less than 15 mM; and
- the osmolality is 250 to 330 mOsm/kg.

[139] As noted, Claim 10 depends on cascading and other dependencies among Claims 1 to 9. Alcon submits that Claim 10 read according to Claims 9, 5, 3 and 1 claims a multi-dose, self-preserved ophthalmic composition comprising:

- travoprost;
- zinc ions between 0.1 to 0.4 mM;

- a borate/polyol complex in which the polyol is propylene glycol and sorbitol;
- wherein the concentration of
    - anionic species < 15 mM
    - multivalent buffering anions < 5mM;
    - multivalent metal ions < 5 mM; and
    - ionized salts < 50 mM.

[140] This reading of Claim 10 is supported by the experts.

XI. CONSTRUCTION OF THE CLAIMS

A. *Jurisprudence and Principles Governing the Construction of a Patent and its Claims*

[141] The principles governing claim construction are well settled.

[142] Justice Hughes provided a useful summary of the relevant principles following a review of all the jurisprudence in *Pfizer Canada Inc v Pharmascience Inc*, 2013 FC 120, [2013] FCJ No 111:

> [64] There have been many judicial instructions as to the construction of a claim. To summarize:
>
> - construction must be done before considering the issues of validity and infringement;
> - construction is done by the Court alone, as a matter of law;
> - the Court is to construe the claim through the eyes of the person skilled in the art to which the patent pertains;

- the Court may obtain the assistance of experts to explain the meaning of particular words and phrases, and as to the state of the art as of the date the claim was published;

- the Court should read the claim in the context of the patent as a whole, including the description and other claims;

- The Court should avoid importing this or that gloss from the description;

- the Court should not restrict the claim to specific examples in the patent;

- the Court should endeavour to interpret the claim in a way that gives effect to the intention of the inventor;

- the Court should endeavour to support a meritorious invention.

B. *What do the Experts say?*

[143] Dr Loftsson provides his opinion on the construction of the claims beginning at para 199 of his affidavit. He defines "multi-dose, "self- preserved" and "anionic species" in the same way as the other experts.

[144] Dr Loftsson notes that Claims 1-9 relate to multi-dose, self preserved ophthalmic compositions, where no active ingredient is specified.

[145] At para 211 Dr Loftsson states that Claim 10 claims a composition of any one of claims 1-9 further containing travoprost as a therapeutically active ingredient.

[146] With respect to Claim 13, Dr Loftsson indicates at para 215 that it covers a topical ophthalmic solution with the following elements:

- 0.004 w/v % travoprost;
- polyoxyl 40 hydrogenated castor oil (i.e. HCO-40);
- a preservative system comprising
    - boric acid,
    - propylene glycol
    - sorbitol;
    - zinc chloride in a concentration of 0.04 to 0.4 mM;
- sodium hydroxide and/or hydrochloric acid to adjust the pH range of the solution to 5.5 to 5.9; and
- purified water;

Claim 13 further requires that:

- the solution is free of benzalkonium chloride (BAK) or another antimicrobial preservative;
- the concentration of the anionic species present in the composition is less than 15 mM; and
- the osmolality is 250 to 330 mOsm/kg.

[147] At para 216 he adds:

> As claim 13 relates to a "solution", this suggests the formulation should be free of particulate matter. The reference to "another antimicrobial preservative" suggests that the formulation does not contain conventional antimicrobial agents (such as those discussed earlier in the patent - e.g. polyquaternium-1).

[148] Dr Miller also provides his opinion on the construction of the claims. He notes at para 71 of his affidavit that Claim 1 includes the following aspects: a multi-dose ophthalmic composition; the composition is self preserved; the concentration of zinc ions in the composition is in the range of 0.04 to 0.4 mM; and, the concentration of anions in the composition is less than 15 mM.

[149] At paragraphs 72-75 he provides his opinion on the meaning of the key terms.

[150] Dr Miller notes, at para 88 of his affidavit, that Claim 10 depends on any one of Claims 1-9 and requires the presence of travoprost as a therapeutically active agent and that it is the first claim in the '370 that specifies travoprost in the composition.

[151] At para 91, Dr Miller describes Claim 13 as an independent claim directed to a topical ophthalmic solution and he sets out the aspects , i.e., the components and limits as he described at para 71.

[152] At para 92, Dr Miller adds:

> Claim 13 includes limitations on the pH (5.5 to 5.9) and osmolality (250 to 330 mOsm/kg) of the ophthalmic solution. The claim also specifically requires that the solution is free of BAC. The remaining elements of claim 13 all appeared previously in one or more of claims 1 to 12 and would have been understood by the skilled person in an analogous manner.

[153] Dr Kent provides a proposed construction of all the claims (as do the other experts). At para 66-68 of his affidavit, he offers the meaning of the terms used, indicating that "multi-dose"

signifies that the compositions require the presence of a preservative, "self-preserved" as defined in the '370 refers to a composition that lacks a conventional antimicrobial preservative, and "ophthalmic composition" would be understood to include such compositions as ocular therapeutic agents.

[154] At para 80 he notes that Claim 10 narrows the compositions of Claims 1-9 to those containing travoprost as a therapeutically active agent and that this is the first claim of the '370 to specifically require the presence of a therapeutically active agent.

[155] With respect to Claim 13, Dr Kent indicates that it pertains to an ophthalmic solution that contains specific components, as set out above (and as indicated by Dr Miller). At para 84, Dr Kent adds:

> Claim 13 relates to topical ophthalmic solutions that are administered topically to the eye. The solutions contain 0.004w/v% travoprost as the active ingredient. Travoprost is said in the 370 Patent to be useful to lower intraocular pressure and treat glaucoma. The solutions also contain a preservative system that includes at least boric acid, propylene glycol, sorbitol and zinc chloride at concentrations from 0.04 to 0.4 mM. These solutions are free of BAK or other antimicrobial preservatives. According to claim 13, the solutions have limited concentrations of anionic species, that is, concentrations of less than 15 mM, and have osmolality values between 250 and 330 mOsm/kg. Finally, the solutions also contain polyoxyl 40 hydrogenated castor oil.

C. *Construction of Claims 10 and 13*

[156] I am tasked with construing the claims at issue in an informed and purposive way through the eyes of the POSITA. I have considered Claims 10 and 13 in the context of the Patent as a whole and with the benefit of the evidence of the experts and the submissions of the parties.

[157] I have also looked at the other claims, which are not at issue, to determine the differences among the claims.

[158] Claim 10 is a formula for a composition and Claim 13 is a formula for a formulation. Nothing more is promised and no proposed use is set out in the claims. In contrast, Claims 11, 12, 14 and 15 refer to the proposed use, i.e., the control of intraocular pressure. Out of 35 claims, only four claims refer to a proposed use.

[159] As Alcon notes, neither Claim 10 nor 13 refers to any reduction in side effects. The Patent suggests that the use of the compositions or formulations for the treatment of certain eye conditions, but the claims at issue do not set out any proposed use.

[160] Of the 35 claims, only two, Claims 13 and 14, are ophthalmic solutions. Neither refers to the particulate matter issue nor to its resolution. It is only the evidence of Dr Loftsson that raises this as part of the construction of the claim and its inventive concept.

[161] Only two of the 35 claims refer to any enhancement; Claims 16 and 35 refer to a method of enhancing antimicrobial activity.

[162] I would construe the claims as follows:

- Claim 13 is an independent claim directed to topical ophthalmic solutions containing travoprost. The solutions also contain a preservative system that includes boric acid, propylene glycol, sorbitol and zinc chloride at concentrations from 0.04 to 0.4 mM.

These solutions are free of BAK or other antimicrobial preservatives. The solutions have limited concentrations of anionic species, that is, concentrations of less than 15 mM, and have osmolality values between 250 and 330 mOsm/kg. The solutions also contain polyoxyl 40 hydrogenated castor oil.

- Claim 10 is a dependent claim which depends on cascading dependencies among Claims 1 to 9. Claim 10 claims a multi-dose, self-preserved ophthalmic composition containing travoprost and a preservative system that includes zinc chloride, propylene glycol and sorbitol, and limited concentrations of anionic species, multivalent buffering anions, multivalent metal ions and ionized salts.

XII. THE INVENTION

A. *Jurisprudence and Principles regarding the Inventive Concept*

[163] In *Apotex v Sanofi-Synthelabo*, 2008 SCC 61, [2008] 3 SCR 265 [*Plavix*] at para 77, the Supreme Court of Canada found that the inventive concept of the claims was not readily discernable from the claims themselves. The Court noted that a bare chemical formula in a claim may not be sufficient to determine its inventiveness and if that is the case, it is acceptable to read the specification in the Patent to determine the inventive concept of the claims. The Court cautioned that "[…] it is not permissible to read the specification in order to construe the claims more narrowly or widely than the text will allow."

[164] In *Abbvie Corporation v Janssen Inc*, 2014 FC 55, [2014] FCJ No 59 [*Abbvie*] at para 123, Justice Hughes emphasized that in applying the four part test set out in *Plavix* to determine obviousness, it is the inventive concept of the claims that must be identified, noting, "The Court

is required to focus on the invention as claimed in the claims at issue, and not on some generalized concept of invention as expressed in the patent as a whole."

B. *Alcon's position on the Inventive Concept*

[165] Alcon submits that the inventors identify two aspects of their invention as stated in the Summary of Invention: (i) the very low concentration of zinc ions and (ii) maintaining a concentration of buffering anions below 15 mM.

[166] Alcon also submits that there are several inventive concepts for Claim 13:

1. Self-preserved solutions of travoprost may be prepared using low concentrations of zinc ions provided the concentration of anionic species is also kept low.
2. Self-preserved solutions of travoprost may be prepared using low concentrations of zinc ions provided the concentration of anionic species is also kept low (i.e. .the solution described in (1)) combined with a borate/polyol system, where the polyol is comprised of sorbitol and propylene glycol.
3. Propylene glycol generates fewer buffering anions than other tested polyols, namely, sorbitol and mannitol. As a consequence, propylene glycol offers advantages when used in a zinc-based preservative system.
4. The pH of a travoprost solution comprising HCO-40 and zinc must be maintained below 6.0 in order to avoid the formation of particulate matter.

These four concepts are based on the evidence of Dr Loftsson.

[167] For Claim 10 (read according to Claims 9, 5, 3 and 1), Alcon submits that the inventive concepts include solutions containing travoprost using low concentrations of zinc and low concentrations of anionic species combined with a borate polyol system where the polyol is propylene glycol and sorbitol and the limits on multivalent buffering anions, metal cations, and ionized salts, all of which impact the efficacy of the zinc-based preservative system.

[168] In response to Apotex's argument that the inventive concept is not consistent with Alcon's assertion of the promised utility, Alcon argues that the inventive concept need not be the same or consistent with the promised utility, noting that the inventive concept is how you get the invention to work whereas the utility is the use of the invention, which is simply an alternative preservative system without BAK.

C. *Apotex's position on the Inventive Concept*

[169] Apotex submits that Alcon's proposed construction of the inventive concept is based on Dr Loftsson's evidence which proposes that each element of the claim should form its own inventive concept and that this also imports information from some of the testing into its fourth inventive concept, regarding the particulate problem. Apotex submits that such a construction is wrong in law.

[170] Apotex submits the inventive concept of the asserted claims is clear; a multi-dose ophthalmic composition containing travoprost employing zinc ions together with a borate/polyol complex, in amounts sufficient to preserve the composition, thereby avoiding the need for a

traditional preservative, such as BAK. The limits on anionic species are not part of the inventive concept, nor is the resolution of the potential particulate problem.

D. *What do the experts say?*

[171] At para 231 of his affidavit, Dr Loftsson expresses the opinion that there are at least four inventive concepts, just as described above at para 166.

[172] Dr Loftsson also provides his opinion on the inventive concept of Claim 10 according to Claim 9 and Claims 5, 3 and 1 in turn due to their dependant nature.

[173] At para 233, Dr Loftsson states:

> In my view the inventive concept of this reading of claim 10 includes concepts a, b and c above. Concept d does not apply as claim 10 does not include a limitation on pH. In addition, claim 10 includes limits on multivalent buffering anions, multivalent metal cations and ionized salts, all of which are disclosed by the inventors to impact on the efficacy of the zinc based preservative system.
>
> (Note: The reference to a, b and c refers to the first three inventive concepts of Claim 13 as set out at para 166).

[174] Dr Loftsson provides an alternative interpretation of Claim 10 according to the composition of Claim 7, and Claims 6, 5, 3 and 1 due to their dependent nature. He indicated that the inventive concept of Claim 10 would be the same except there would be no limit on iodized salts.

[175] On cross-examination, Counsel for Apotex raised several of the "further enhancements" noted at page 5 of the Patent. Dr Loftsson agrees that the reference to "the present invention can be further enhanced by the use of zinc ions in combination with borate or a borate/polyol complex" is an "add on" or "another bell and whistle". Dr Loftsson also agrees that the paragraph beginning at line 25 which states that the performance of the zinc-based preservative systems of the present invention is further enhanced by limiting the amount of multivalent metal cations other than zinc and limiting the amount of ionised salts are also other "bells and whistles".

[176] Counsel for Apotex continued to question Dr Loftsson in this manner at Q 399-406 and Dr Loftsson agrees that the inventors are not saying that "you need these bells and whistles to meet the needs of the invention" but rather that these are "additional bells and whistles to give you more of an enhancement".

[177] Apotex's expert, Dr Miller refers to the inventive concept of a range of claims, and notes at para 168 of his affidavit:

> In my opinion, the inventive concept of claims 1 to 15 and 28 to 34 of the '370 Patent is multi-dose ophthalmic compositions employing zinc ions, in some cases together with a borate or a borate/polyol complex, in amounts sufficient to preserve the composition, thereby avoiding the need for BAC. By not employing BAC in the compositions, any possibility of side effects experienced by certain patients when exposed to this preservative are avoided.

[178] In his summary of opinions, Dr Kent states at para 22 of his affidavit:

> In my opinion, the inventive concept of the claims of the 370 Patent relates to multi-dose ophthalmic compositions containing

> zinc ions in relatively low concentrations as preservatives instead of conventional preservatives such as benzalkonium chloride ("BAK") in order to avoid the deleterious side effects on the cornea caused by BAK. In some cases, the compositions also comprise borates and polyols.

[179] At paras 95 and 140, Dr Kent sets out the inventive concept as noted above and adds:

> Further, as the 370 Patent explains, BAK was historically commonly used in ophthalmic compositions, but it was known to cause ocular side effects in certain subsets of patients. By replacing BAK in the compositions with zinc ions (and optionally borates and polyols), the threat of these BAK-related side effects is precluded. In my opinion, this represents an aspect of the inventive concept of the 370 Patent.

E. *The Inventive Concept*

[180] The claims themselves provide bare chemical formulas which do not permit identification of the inventive concept without looking at the specification.

[181] As noted in *Abbvie*, above, the focus is on the invention as claimed in the claims at issue, i.e. Claims 10 and 13, and "not on some generalized concept of invention as expressed in the patent as a whole."

[182] I note that the disclosure of the Patent repeats several times the key sentences of the Summary of the Invention. I also note that Alcon highlighted two aspects of the invention, the low concentration of zinc ions and maintaining the concentration of buffering anions at less than 15 mM, both of which are found in the Summary.

[183] The detailed description of the invention which begins at page 6c first sets out the limits for the zinc ions, indicating a preference for zinc chloride. It then notes that "it is preferred that" the total concentration of anionic species in the compositions should be limited, "to an amount of less than 15 mM, *more preferably* less than 10 mM, and *most preferably* less than 5 mM". It then proceeds to refer to many other preferences with respect to the components. For example, at page 9, the Patent indicates that propylene glycol is *particularly preferred* in order to limit the presence of anionic species and that a borate polyol complex is *preferred* and a propylene glycol or combination of propylene glycol and sorbital is *most preferred*.

[184] The Patent continues to set out other enhancements, methods and possible uses at the pages that follow.

[185] The reference that Alcon relies on to support the additional inventive concept of a particular pH range to ensure against particulate matter is found at page 14.

[186] While that paragraph is directive in indicating that where cationic or anionic excipients are used, the amount must be limited and the pH range "needs to be in the range of 5.0 to 6.0, preferably in the range of 5.5 to 5.9", the nature of this paragraph is similar to many other paragraphs in the Patent detailing the various enhancements and options that are not asserted to be inventive concepts.

[187] Although Alcon argues that the inventive concepts are set out "in spades" across the Patent, I am not persuaded that some of the preferences should be regarded as inventive concepts

but not others. If a reference at page 14 is an inventive concept, then should several other references which appear to have the same level of significance similarly be inventive concepts, or should none of them be inventive concepts?

[188] As noted, the key aspects set out in the Summary of Invention are repeated several times, suggesting that the inventive concepts are highlighted in that summary.

[189] Apotex takes the position that the inventive concept is simply a multi-dose ophthalmic composition using zinc ions with, in some cases, or optionally, a borate polyol complex in amounts sufficient to preserve the composition and without BAK.

[190] Alcon takes the position that each aspect of the formula set out in the claims is a separate inventive concept and also that the resolution of the particulate problem is an inventive concept.

[191] The inventive concept lies somewhere between these two positions but each aspect of the formula is not a separate inventive concept.

[192] Only Dr Loftsson attached significance to the reference at page 14 regarding the possible particulate problem and how it could be resolved. However, he also indicates in his affidavit that the POSITA would know how to address the problem. The other experts also clearly indicate that a POSITA would know how to address the particulate problem. So if it is a problem, it would not be inventive to resolve the problem. Therefore, I cannot conclude that resolving the particulate problem is part of the inventive concept.

[193] Dr Loftsson also agreed, when the proposition was put to him, that other preferences or enhancements were "bells and whistles". For example, he indicated that using zinc in combination with a borate/polyol complex was "another bell and whistle". The other experts appear to agree that the combination of zinc and a borate polyol complex is preferred. Dr Miller refers to "in some cases together with a borate or a borate/polyol complex" and Dr Kent says "optionally borates and polyols".

[194] Overall, the expert evidence is not particularly helpful in identifying the inventive concept.

[195] The bare chemical formulas of claims 10 and 13 are specific in setting out the ingredients or elements of the composition or formulation and the applicable concentrations or limits where these are essential, for example, the concentration of zinc chloride and anionic species and the range for osmolality and pH levels.

[196] The Summary of Invention notes that certain formulation parameters must be maintained in order to utilize low levels of zinc ions. The Summary refers to the pH and osmolality values and to the need to limit the concentration of buffering anions to less than 15 mM. I attach significance to these elements which were repeated several times in the Patent.

[197] I find that the inventive concept includes these essential aspects. The Inventive Concept is a (self-preserved) multi-dose ophthalmic composition or formulation containing travoprost that does not include BAK and which uses a non-conventional preservative system that includes low

levels of zinc chloride, a borate/polyol complex (or propylene glycol and sorbitol), low levels of anionic species (less than 15 mM) and specific osmolality values.

XIII. OBVIOUSNESS

[198] There is no disagreement about the legal principles that apply to the determination of obviousness. The disagreement is about how the test established in *Plavix* applies to the facts of this case.

[199] The parties' positions regarding obviousness follow from their respective views of the inventive concept, which differ, and from their view of the teachings of the prior art, which also differ.

[200] Alcon argues that there were differences in the state of the art and common general knowledge and the inventive concept, and that these differences were not obvious because they were not self-evident, and that Alcon's efforts to reach the invention were significant.

[201] Apotex argues that there are no differences between the inventive concept of the claims and the prior art and common general knowledge because the prior art taught the elements of the invention and the combination of those elements. Apotex notes that the preservative system in Systane Free was particularly relevant and, given the existence of DuoTrav and Travatan, it would have been self-evident to start with these formulations and switch the preservative system to that of Systane Free or a similar system. To the extent that there are differences, Apotex

argues that these were self-evident for the POSITA and that the invention would have been reached as a matter of routine experimentation.

A. *Jurisprudence and Principles on Obviousness*

[202] The Supreme Court of Canada stated the current law on obviousness in *Plavix*, at para 67-69. Justice Rothstein followed the four step approach that originated in *Windsurfing International Inc v Tabur Marine (Great Britain) Ltd*, [1985] RPC 59 (CA) and was updated in *Pozzoli SPA v BDMO SA*, [2007] FSR 37, [2007] EWCA Civ 588 (BAILII). The four steps direct the Court to:

1. Identify the notional "person skilled in the art", i.e. the POSITA, and the relevant common knowledge of the POSITA as of the claim date;
2. Identify the inventive concept of the claim in question or if that cannot readily be done, construe it;
3. Identify what, if any, differences exist between the matter cited as forming part of the "state of the art" and the inventive concept of the claim or the claim as construed; and,
4. Determine whether these differences, viewed without any knowledge of the alleged invention as claimed, constitute steps which would have been obvious to the person skilled in the art or would have required any degree of invention.

[203] At this fourth step, an “obvious to try” test may be considered. Justice Rothstein identified a non-exhaustive list of relevant considerations to assess whether it would be obvious to try to reach the invention, at para 69:

(1) Is it more or less self-evident that what is being tried ought to work? Are there a finite number of identified predictable solutions known to persons skilled in the art?

(2) What is the extent, nature and amount of effort required to achieve the invention? Are routine trials carried out or is the experimentation prolonged and arduous, such that the trials would not be considered routine?

(3) Is there a motive provided in the prior art to find the solution the patent addresses?

[204] Other relevant factors may include the history of the invention, whether the inventor arrived at the invention quickly and easily based on the prior art and common general knowledge, and the inventors' particular expertise compared to that of the skilled person (at para 70-71).

[205] The Federal Court of Appeal in *Apotex Inc v Pfizer Canada Inc*, 2009 FCA 8, [2009] FCJ No 66 at para 29 emphasized that possibility and speculation is not the test, nor is "worth a try"; the invention must be more or less self-evident.

[206] Hindsight may not be used to assess whether an invention was obvious to try as tempting as such an approach may be (*Beloit Canada Ltd v Valmet Oy* (1986), [1986] FCJ No 87, 8 CPR (3d) 289, 64 NR 287 at para 21).

[207] In *Abbott Laboratories v Canada (Minister of Health)*, 2008 FC 1359, [2009] 4 FCR 401, aff'd 2009 FCA 94, [2009] FCJ No 345 [*Abbott*], at para 59, Justice Hughes clarified the distinction between obviousness and anticipation, noting that both are questions of fact and both are informed by the prior art, but the tests differ. For anticipation, a single disclosure is the focus

and the issue is whether it would have been considered by a POSITA to disclose and enable the claimed invention. For obviousness, if there are differences between the disclosure, the issue is whether the POSITA would have been expected to reach the invention without exercising inventive ingenuity. If so, the invention is obvious. If there is room for inventive ingenuity, it is not obvious.

[208] Allegations of obviousness, unlike anticipation, do not focus on a single disclosure but on the mosaic of the relevant prior art and the common general knowledge. (See *Shire Biochem Inc v Canada (Minister of Health)*, 2008 FC 538, [2008] FCJ No 690 at 76-78 citing *Rothmans, Benson & Hedges Inc v Imperial Tobacco Ltd* (1993), 47 CPR (3d) 188, [1993] FCJ No 135 (FCA) at pages 197-199).

B. *Alcon's position on Obviousness*

[209] Alcon submits that in the application of the *Plavix* test to the present case, there were several differences between the prior art and the inventive concepts of the claims. In assessing the obvious to try test at the fourth step, the invention of the '370 was not self-evident and Alcon's efforts to reach the invention required experimentation which was not routine.

[210] Alcon argues that there are four inventive concepts for Claim 13 (as noted above at para 166) including its resolution of the possibility of particulate matter forming in solutions. Alcon focuses on the specific requirements of the composition and formulation and the combination of the elements as well as the need to maintain low levels of anionic species noting that these were not taught by the prior art.

[211] Alcon maintains that the elements and combination of elements within specified ranges are not "bells and whistles", but key parts of the inventive concepts.

[212] Alcon argues that the prior art relied on by Apotex did not disclose: the formulations claimed by Claims 13 or 10; the low levels of zinc combined with the limit on anionic species; the limits on multivalent metal cations and buffering ions, or ionized salts; the advantages of propylene glycol in the preservative system; or, the particulate problem.

[213] Alcon submits that these differences would not have been obvious to the POSITA.

[214] Alcon argues that the prior art showed other options to enhance antimicrobial activity. In addition, there was no motivation in the prior art to select zinc in preference to these other options. Alcon also argues that the prior art, particularly Xia and Kiyobayashi, did not teach the use of zinc at low concentrations.

[215] With respect to the limit on anionic species, Alcon argues that the prior art did not teach that the anionic species limit should be kept lower than 15 mM in a zinc-based system. Xia and Kiyobayashi provide no guidance on the anionic species limits; rather formulations with higher levels of anionic species are taught.

[216] Alcon notes that the Chowhan Patent #2 teaches that a specific buffering anion (phosphate) reduces the antimicrobial activity of preservatives (which do not include zinc) but does not teach anything about preservatives that include zinc.

[217] Alcon also argues that the reliance on McCarthy is misplaced as it teaches reactions regarding the precipitation of salts, whereas the '370 deals with ions in solution. Alcon submits that McCarthy is an old and non-specific reference which provides only a suggestion about anions without any guidance about the levels of anionic species. Alcon again notes that the NOA did not indicate that McCarthy would be relied on by Apotex as teaching the limit on anionic species despite that Apotex knew that anionic species were an element of the claim.

[218] With respect to Systane Free, Alcon submits that if the particulars are found by this Court to be within the scope of Apotex's Notice of Allegations these must be considered in the context of the other art which teaches the use of higher amounts of zinc. Alcon also argues that Systane Free is a different formulation and it does not make the present invention obvious. Therefore, it was not obvious to try, i.e., to switch the Systane Free preservative system into Travatan. Although Systane Free contains zinc and other similar components, it is a different system with different ingredients, different pH level (7.9) and anionic species above the specified mM level.

[219] Alcon also disputes Apotex's position that the invention is the result of routine experimentation, arguing that there would be no reasonable expectation of success that the Systane Free system would work in Travatan and the prior art does not teach that the anionic species concentration is a factor for the zinc-based preservative system.

[220] Alcon also argues that the prior art did not direct the POSITA to a borate/propylene glycol/sorbitol combination or that the selection of propylene glycol would generate fewer anions than sorbitol (which Alcon refers to as the propylene/glycol advantage. Alcon notes that

there was a single reference to propylene glycol in Xia but it was not preferred. Similarly in Chowhan, there was no teaching to enhance the activity of zinc.

[221] Alcon emphasizes that one of the significant inventive differences is the combination of components, which had not been taught and was not obvious. Alcon argues that Apotex points to individual ingredients in the prior art but this is not sufficient to teach the use of that ingredient in combination with the others or at the required levels of the invention. Apotex notes that the "obvious to try" branch of the *Plavix* test demands that there is a reasonable or fair expectation of success and that there was no such expectation. A POSITA would have to experiment. Many factors impact on antimicrobial activity and it is difficult to attribute a change in preservative efficacy to a change in the formulation when several changes are made. This would take the POSITA farther away from an expectation of success.

[222] Alcon points out that Apotex's witness, Dr Kent, agreed that in the absence of testing, the POSITA would not know whether the preservative effect of combining borate/polyol complexes and zinc would add to or reduce the preservative effect.

[223] With respect to Claim 10, Alcon notes that the claim has several species limits and none were disclosed in the prior art.

[224] Alcon also argues that nothing in the prior art indicated the potential particulate problem or taught how to resolve it. Alcon submits that as a result of its own experimental work, the problem was solved.

[225] Alcon points to Dr Kent's evidence that he was not aware of products using other alternative preservative systems, only Travatan Z. Alcon also notes that others were working in the field but didn't get to this invention.

[226] Alcon also argues that there were several possible approaches to reach the invention and it expended considerable effort to develop the invention.

C. *Apotex's position on Obviousness*

[227] Apotex argues that the common general knowledge regarding the development of ophthalmic compositions and formulations together with the state of the art would collectively direct the POSITA to the invention.

[228] Apotex also relies on the teachings of the Xia and Kiyobayashi applications, the Chowhan Patents #1, #2 and #4 and the evidence of Dr Miller and Dr Kent to support its submission that zinc was a known preservative, borate/polyol complexes were known preservatives, acceptable pH and osmolality ranges were known and, that the prior art provided additional support for the existing common general knowledge that the lowest possible quantities should always be used.

[229] Apotex also submits that Travatan and DuoTrav, both containing travoprost as the therapeutic ingredient and both preserved with BAK, were marketed by Alcon at that time and their compositions were known.

[230] Apotex points out that Dr Chowhan is a co-inventor of the present invention, but that Alcon did not tender any evidence from Dr Chowhan.

[231] With respect to the *Plavix* test, Apotex submits that the differences between the prior art and common general knowledge and the inventive concept, which Apotex maintains is a multi-dose ophthalmic composition containing travoprost employing low concentrations of zinc ions together with a borate/polyol complex in amounts sufficient to preserve the composition, thereby avoiding the need for a traditional preservative such as BAK, were self evident.

[232] Apotex submits that Claims 10 and 13 encompass self-preserved multi-dose ophthalmic compositions comprising travoprost, a zinc-borate-sorbitol-propylene glycol complex and additional "bells and whistles" which are not part of the inventive concept.

[233] As noted above, Apotex argues that the anionic concentration limit is not part of the inventive concept. Apotex notes that Dr Loftsson on cross-examination agreed that the Patent's reference to limiting the anionic species was one of several further enhancements.

[234] Apotex maintains that the differences between the state of the art, the common general knowledge and the invention were self-evident even if the limits on anionic species are part of the inventive concept.

[235] Apotex points to the very relevant prior art, particularly Travatan, preserved with BAK and Systane Free, preserved without BAK, as a key example that the difference between the state

of the art and the present invention was self-evident. All that was needed was to switch the BAK with the non-conventional preservative system used in Systane Free. Apotex argues that there was more than a reasonable expectation that this would provide an effective preservative for the formulation.

[236] Apotex notes that Systane Free was Alcon's own product which was on the market in 2005 and 2006. Systane Free did not use a traditional preservative system but instead used an ionic buffering system which included zinc, and a borate/polyol complex, which included propylene glycol and sorbitol. Apotex notes that Alcon promoted and disclosed Systane Free, including at the ARVO conference in 2006 through its poster presentations. In addition, a POSITA could have analysed the product to determine its composition. Apotex notes that the preservative system of Systane Free is very similar to that of Claim 13.

[237] The POSITA, being aware of the state of the art and possessing the common general knowledge would use their skills and would immediately look to Travatan as the starting point to formulate an ophthalmic composition without the side effects of BAK. The POSITA knows how to formulate ophthalmic compositions and knows that the principle is to change as little as possible from Travatan. The POSITA would also know that there were only a few non-conventional preservative systems, one of which was the preservative system in Systane Free, which was a zinc-borate/polyol complex preservative system. Apotex notes that zinc was a well-known preservative as were borate/polyol complexes.

[238] Apotex notes that there was motivation to avoid toxicity, irritation and damage to ocular surface and to replace BAK because it was associated with these side effects.

[239] Apotex argues that the focus of the obviousness inquiry is to determine whether the decision to replace BAK with the preservative system used in Systane Free, or a very similar system, and the subsequent routine testing and optimization that Alcon conducted required the exercise of inventive ingenuity or whether it was routine work of the ordinary skilled person.

[240] Apotex notes that Alcon did not lead any evidence of differences in the preservative systems. Apotex argues that the differences *alleged* by Alcon are not supported by the evidence. The same combination of formulation components, i.e., zinc, borate, sorbitol and propylene glycol, is in both the preservative system in Systane Free and the preservative system of the '370.

[241] Apotex also notes that Alcon indicated, in its letter to physicians following the removal of Systane Free from the market in 2006, that Travatan Z was not affected and that the preservative system in Travatan Z (the present invention) was an extension of the borate/polyol preservative system used in Systane Free.

[242] Apotex also notes that Dr Loftsson agreed on cross-examination that Travatan contained many of the same components as the '370 (i.e., with respect to the preservative system).

[243] Apotex also disputes that the "propylene glycol advantage" is part of the inventive concept, but submits that if it is, the POSITA would know that this was part of the preservative system of Systane Free.

[244] Apotex submits that faced with Systane Free, its own product, Alcon cannot take the position that there was no teaching in the prior art of such a preservative system.

[245] Apotex argues that there was only one non-inventive difference between state of art and inventive concept. The prior art disclosed Travatan, which was an ophthalmic composition containing travoprost as the active ingredient with BAK as the preservative. The prior art also disclosed Systane Free, which was an ophthalmic composition without an active ingredient and with a non-conventional zinc and borate/polyol preservative system. Apotex argues that the difference was replacing the BAK in Travatan with the preservative system in Systane Free. This was self-evident and non-inventive and, therefore, obvious.

[246] Although Apotex disputes that the anionic concentration limit is part of the inventive concept, Apotex submits that if the limit on anions were part of the inventive concept, arriving at the limit merely required routine work that is done when optimising a preservative free composition.

[247] In response to Alcon's argument that nothing in the prior art disclosed 15 mM as the upper limit on anionic species, Apotex submits that a reference to a single disclosure or one piece of the prior art is an anticipation approach and that an invention is obvious based on the

mosaic of prior art and the common general knowledge. The common general knowledge is that the lowest concentrations should always be used.

[248] Apotex argues that there is nothing inventive about Alcon optimizing the concentrations of anionic species. The prior art would have directed the POSITA to limit the concentration of anions; for example, McCarthy taught that the anti-microbial activity of zinc is inhibited by the presence of multivalent metal cations and anionic species such as hydroxide ions.

[249] Apotex argues that although Alcon seeks to avoid the teachings of McCarthy by arguing that Apotex did not cite McCarthy in the NOA for this purpose, Apotex is permitted to respond to evidence led by Alcon. Alcon's expert, Dr Loftsson expressed the opinion that the anionic species formed part of the inventive concept. Although McCarthy only provides a general teaching, it is part of the mosaic of art and it informs the POSITA.

[250] With respect to the particulate problem, Apotex maintains its position that overcoming the particulate problem is not part of the inventive concept. Alternatively, Apotex submits that it was not inventive for Alcon to resolve this problem because the POSITA would have known exactly what to do. Apotex's expert, Dr Miller indicated that there were two approaches - either adjust the pH level or purchase a better grade of HCO-40. Overcoming this problem was routine as evidenced by Dr Kabra who worked for Alcon and whose lab book demonstrates that the problem only took a few days to resolve and who described the changes to pH as minor adjustments.

[251] Apotex also responds to Alcon's argument that combining the components is a key aspect of the invention and that nothing taught this combination or predicted that it would work. Apotex argues that there was nothing left to predict; the same components had already been combined in Systane Free and the follow up, i.e., the preservative efficacy testing, was routine.

[252] Apotex again notes that in assessing obviousness, the focus is not on individual pieces of prior art but on the entire relevant prior art. The POSITA would have the specific teachings of Systane Free and Travatan as well as the general teachings of a range of other art in hand along with their common general knowledge and their skills.

[253] Apotex also submits that there was motivation to find an alternative preservative system to replace BAK, given its side effects.

[254] More generally, Apotex submits that Alcon has not met its burden to show that Apotex's allegations of invalidity on the ground of obviousness are not justified. Apotex submits that it has led evidence, including that the POSITA would look to the non-conventional preservative system in Systane Free to replace BAK in Travatan (or other ophthalmic compositions), and this evidence is sufficient to put the issue into play. Apotex submits that the evidence of Dr Loftsson must be carefully scrutinised because he did not understand the concept of obviousness and he was instructed to ignore the details of Systane Free as part of the prior art.

D. *What do the experts say?*

(1) Doctor Loftsson

[255] Dr Loftsson provides a detailed affidavit which includes his review of the prior art referred to in the Patent and in the NOA. He also provides a detailed opinion on the disclosure of the Patent and what each example and Table reveals.

[256] Dr Loftsson's opinion on obviousness is set out at para 249-250. He notes the questions he has been asked to consider which reflect the elements of the *Plavix* test.

[257] Dr Loftsson identifies the common general knowledge as of September 2006 at para 253 of his affidavit as including the following: BAK was a commonly used anti-microbial preservative in multi-dose ophthalmic formulations (and he identifies five other examples of preservatives in use at the time); long standing concerns existed about the use of BAK; other agents including zinc and other metal ions, sorbic acid and boric acid, were known to have some preservative enhancement; buffers in ophthalmic solutions included borates, phosphates, citrates and acetate; and, multivalent buffers were commonly used.

[258] At para 255, Dr Loftsson identifies the differences between the state of the art and the inventive concept of the claims. His opinion of the differences is based on the four or more inventive concepts which he identifies at para 229-231 of his affidavit (as set out above at para 166). Dr Loftsson expresses the opinion that the inventive concepts were not known in the prior art as of 2006. He states:

> In particular the state of the [*sic*] did not describe:
>
> - the claim 10 or 13 formulations;
> - the low levels of zinc used for preservation;
> - the limit on anionic species;
> - the limits on multivalent metal cations, multivalent buffering anions or ionized salts;
> - the advantages of propylene glycol in the preservative system; or
> - the particulate problem encountered during development.

[259] At para 256-257 he expresses his opinion that these differences would not have been obvious to a POSITA and would have required a degree of invention. He states that the POSITA would have to make decisions about several formulation parameters including the pH level, noting that Travatan was formulated at a pH of 6.0 and the POSITA would start there. In addition, decisions would be needed regarding the tonicity, buffer selection, solubilizer or surfactant and the preservative. He adds that introducing a new ingredient may change the pH or create unforeseen interactions with other formulation components.

[260] Dr Loftsson states that there was no motivation to select zinc in the prior art and that if zinc were selected, the prior art suggested its use at higher levels. With respect to anionic species limits, Dr Loftsson states at para 263 that nothing in the prior art suggests that the anionic species should be below 15 mM in a zinc-based system. He notes that the Xia examples have higher anionic species and Kiyobayashi has no limits.

[261] At para 265-271 Dr Loftsson acknowledges that the prior art describes the use of borate/ polyol systems to enhance preservation, but that nothing indicates that this was the preferred choice. He adds that the combination of propylene glycol, sorbitol and boric acid would have required experimentation.

[262] With respect to Alcon's reference to the "propylene glycol advantage", Dr Loftsson notes at para 271-273 that the use of propylene glycol allows the inventors to use lower levels of sorbitol while maintaining the balance of buffering capacity, tonicity and preservation and that this advantage "is not discussed in the prior art cited by Apotex".

[263] Dr Loftsson refers to the particulate problem at para 275. He notes that Claim 13 provides the inventors' solution to the problem, which was to adjust the pH. He adds that in hindsight this may seem to be a simple solution, but it would not have been obvious to a POSITA for several reasons. He explains that identifying the source of the problem required significant work, which was described by Dr Kabra. He notes that adjusting the pH would require experimentation and the POSITA would not know whether it would work.

[264] He also adds that some precipitate problems cannot be solved.

[265] With respect to multivalent buffering anions, multivalent metal cations and ionized salts in Claim 10, Dr Loftsson states that the prior art did not describe the limits in conjunction with the use of zinc.

[266] Dr Loftsson expresses his opinion at para 282-283 that it would not be more or less self-evident that the invention would work because the complex preservation system was new and, given the possible combination of ingredients for ophthalmic formulations, there was not a finite number of solutions known to the POSITA. He adds that it would not have been self-evident to lower the pH to address the particulate problem.

[267] With respect to the amount of effort required to achieve the invention, Dr Loftsson states at para 284 that the actual laboratory work to prepare and test new formulations for travoprost and its microbial preservation would not be arduous. He adds that preservative efficacy testing is more time consuming but this testing is routine and "largely automated".

[268] He also notes at para 287 that based on his review of Dr Kabra's affidavit, the preparation and testing of the invention was substantial.

[269] With respect to motive, Dr Loftsson notes at para 286 that "there was a desire in the art to remove BAK (and similar preservatives) from ophthalmic formulations. However, the continued long use of BAK in ophthalmic formulations as a common excipient is consistent with the difficulties in developing formulations that eliminate BAK." (I interpret this to mean that BAK continues to be used because it is difficult to find an alternative.)

[270] Dr Loftsson was extensively cross-examined on his opinion.

[271] In response to Q 207-214 regarding the Person Skilled in the Art, Dr Loftsson appears to understand that the analysis of obviousness is to be done from the perspective or through the eyes of the POSITA, but he also indicates that he was such a person. He expresses his opinion on obviousness from his own perspective "more or less".

[272] At Q 212-213, he agrees that in assessing obviousness, he asked himself whether he, i.e., as Dr Loftsson, would think it is obvious.

[273] At Q 194-197, Dr Loftsson answers that he was not familiar with the concept of obviousness according to Canadian law, and he has "difficulty sometimes to understand that, […]". He notes that he had discussions with counsel for Alcon about the concept, but then indicates, "About the Canadian system, yes, and even if they have told me something, I tend to forget, because I don't remember it."

[274] In response to questions regarding his understanding of his mandate to assess obviousness, Dr Loftsson indicates at Q 197 that he understood that obviousness had to be assessed from a particular date, but adds "Isn't it by the time of the filing of the patent?" In response to further questioning, he indicates that he conducted his assessment of obviousness as of that date (the date of filing of the patent), which was September 2007. (I note that the obviousness inquiry should be assessed as of September 2006.)

[275] At Q 670-671 Dr Loftsson agrees that he found different inventive concepts for Claims 10 and 13 and that one of the differences between the state of the art and the inventive concept is

the precise formulation of those claims. He also indicates that this position is consistent with his understanding that in determining whether something is obvious you look at whether it is new.

[276] With respect to Systane Free, Dr Loftsson indicates at Q 736-748 that he was not provided with the composition details of Systane Free and that he did not ask for those details, although he was aware of the product. After first indicating that he did not remember, he then agrees that counsel for Alcon had asked him not to consider the composition details for Systane Free, and also responds that this did not bother him.

[277] He further agrees that he did not take into account any knowledge the skilled person would have had about the composition details of Systane Free because of the request to not consider those details.

[278] At Q 683, Dr Loftsson agrees that to develop a new formulation of travoprost not containing BAK the formulator would look at the existing Travatan formulation as a starting point.

[279] At Q 691-716, Counsel for Apotex directs Dr Loftsson to several articles identified by footnotes in Dr Loftsson's opinion which Dr Loftsson agrees he had relied on in reaching his opinion, several of which were published after September 2006 and a few as recently as 2012.

[280] At Q 706, with respect to the use of zinc as a preservative, Dr Loftsson indicates that he looked to the literature on the issue of the minimum inhibitory concentration needed and he

found the information in a 2011 publication. He responds to Q 707 that he looked for this information in the pre-2006 literature but didn't find it, noting "it could be there. This was what I found, and I used it."

(2) Doctor Miller

[281] Doctor Miller provided a detailed opinion on obviousness with a summary at para 30 of his affidavit indicating that for each chemical component that appears in Claims 1-15 and 28-34, there were examples of its use in the prior art teachings for the same purpose. He adds that there was no information in the prior art that the components would be incompatible in an ophthalmic composition.

[282] With respect to Systane Free, Dr Miller states that "knowledge of the composition of the Systane product would reveal that a number of them, (zinc chloride, boric acid, propylene glycol and sorbitol) had already been successfully formulated together."

[283] As noted above, Dr Miller is of the opinion that the inventive concept of the claims (i.e., Claims 1-15 and 28-34) is multi-dose ophthalmic compositions employing zinc ions, in some cases with a borate or borate/polyol complex in amounts sufficient to preserve the composition, thereby avoiding the need for BAK. He adds that avoiding BAK would avoid the side effects associated with BAK.

[284] At para 32 he concludes his summary on obviousness indicating that relying on the teachings of the prior art, the skilled person would have arrived at the subject matter of the

claims "without requiring inventive activity. Rather, the claimed compositions were self-evident to a skilled person and would naturally flow from an optimization process using only routine experimentation."

[285] Dr Miller reviews the components of the invention and refers to the prior art which addressed each of those components in detail in his affidavit.

[286] At para 201 he indicates that each of the elements of Claim 13 that are present in any one of Claims 1-12 have precedence in the prior art and would have been known to a skilled person.

[287] Similarly, he concludes at para 191 that there is no difference between the elements of Claims 10-12 and what was known in the art as of September 21, 2006, noting that if there were any differences, they would have been self-evident to the skilled person.

[288] At paragraphs 217-245, Dr Miller reviews the common general knowledge and the state of the art, and notes, among other things:

- As of September 2006 there were many strategies known for preserving ophthalmic formulations and preventing microbial contamination;
- Long before 2006 there had been a shift away from traditional preservatives to alternatives that were less harsh to the eye;
- The use of zinc as an antimicrobial was known as an effective strategy and Xia, Kiyobayashi and the Systane product are leading examples of this approach;

- The use of borate/polyol complexes was also known and the Chowhan '799 Patent is an example;
- Xia and Kiyobayashi were significant teachings regarding low concentrations of zinc ions;
- The skilled person would know that the use of low concentrations of anionic species and ionized salts in the travoprost compositions disclosed in the '370 were self-evident due in particular to the teachings of Chowhan and Xia;
- The skilled person would have been motivated to keep the concentration of anionic species as low as possible to avoid decrease in antimicrobial activity in light of the low zinc concentration;
- The use of travoprost in the claims at issue is not inventive due to the existence of Travatan and Duotrav, combined with the teachings of Xia and Chowhan;
- A skilled person would have had reason to optimize the amounts of borate/polyol, propylene glycol and sorbitol as disclosed in Chowhan ('799 Patent) because these were "result-effective variables known to affect the properties of the composition" and "[t]he ability to optimize these amounts was straightforward work that was done routinely by the skilled person prior to September 21, 2006";
- The Systane product is another example of a zinc-based preservative system including zinc, boric acid, propylene glycol and sorbitol;
- The pH of an ophthalmic composition was known to affect the antimicrobial activity (e.g. the Chowhan '799 Patent would have directed the skilled person to optimize the pH within a range of 4-8 typically);

- The skilled person would recognize that a solution to the particulate problem would be to adjust the pH level; and,
- Motivation for the skilled person to develop the invention existed from the prior art which provided "ample precedents".

[289] Dr Miller also comments on Dr Loftsson's affidavit regarding obviousness, particularly the teachings of the prior art and disagrees with his conclusions. Dr Loftsson's opinion was based on his view of the four or more inventive concepts as including the particulate matter problem and solution. Generally, Dr Miller comments that Dr Loftsson has misinterpreted some of the teachings of the prior art, including Xia and Kiyobayashi.

[290] Dr Miller notes at para 277, that the particulate issue should not be elevated to an inventive concept beyond its relative importance to the invention of the Patent. Dr Miller also notes at para 265 that Dr Loftsson's analysis ignores the existence of the Systane product that relied on zinc ions at a concentration that falls within the claimed range.

(3) Dr Kent

[291] Dr Kent also provides an extensive opinion on the state of the art and common general knowledge and the specific teachings of the prior art.

[292] He summarizes his opinion on obviousness at paragraph 25 of his affidavit indicating that any differences between the state of the art and the inventive concept of Claims 1-15 and 28-34 of the '370 were self evident or plain. Dr Kent's opinion is generally based on his view that the

inventive concept is a multi-dose ophthalmic composition containing zinc in low concentrations as preservatives instead of conventional preservatives such as BAK in order to avoid the side effects caused by BAK.

[293] At paragraphs 99-184, Dr Kent comments on the specific teachings of the prior art including Xia, Kiyobayashi, the Travatan product monograph, the DuoTrav product monograph and the four Chowhan patent applications.

[294] Dr Kent notes at para 121 that the Xia application does not include an explicit discussion of the amount of anionic species in the composition. He explains, however, that there was no teaching in Xia that the compositions require concentrations in excess of 15 mM. He says, "In other words, the compositions described in Xia et al include those with a concentration of anionic species of less than 15 mM."

[295] At para 139, Dr Kent notes that Kiyobayahsi disclosed compositions containing anionic species, buffering anions, multivalent cations or ionized salts but did not include an explicit discussion of the levels for these components. He adds, "Nevertheless, Kiyobayashi included guidance against using amounts of excipients that would conflict with the preservation characteristics of the compositions."

[296] Dr Kent's opinion on obviousness includes his consideration of the teachings of the prior art as it relates to a range of claims (Claims 1-15 and 28-34). Dr Kent then provides his opinion on the specific claims at issue.

[297] With respect to the teachings of Xia, Dr Kent notes at para 143-147 that Claim 13, which includes travoprost as the active ingredient with specific pH levels and osmolality values, were all contemplated by Xia. He states "Xia et al contemplated ophthalmic compositions having physicochemical parameters consistent with the subject matter of claim 13 […]".

[298] Dr Kent also concludes at para 151 that Kiyobayashi disclosed ophthalmic compositions having physicochemical parameters consistent with the subject matter of Claim 13.

[299] At paragraphs 185-193, Dr Kent addresses the teachings of the Systane Free product and sets out its compositions. He expresses the opinion that the POSITA with knowledge of the components of Systane Free would recognize that the zinc ions derived from zinc chloride at a concentration equivalent to 0.11 mM was the primary preservative. He adds that the POSITA would have understood, based on the Chowhan patents, that borate/polyol complexes would also exhibit antimicrobial activity to supplement that provided by zinc ions. Dr Kent also notes that a POSITA would have been able to ascertain this information from a sample of the product.

[300] Dr Kent also addresses the teachings of the McCarthy articles, at para 194-199, noting that these include several points salient to the '370.

[301] Dr Kent structures his detailed opinion on the obviousness of Claims 1-15 and 28-34 and concludes that there are precedents in the prior art for each of the elements that form part of these claims. He groups the elements into three categories and analyzes the prior art relating to each category: chemical compounds (e.g. zinc ions, borate, polyols, travoprost); chemical species to

be limited (e.g. less than 15 mM of anionic species); and, physicochemical parameters (e.g. pH and osmolality).

[302] At para 203 he expresses the opinion that each of the chemical compounds that are included in Claims 1-15 and 28-34 was known to the POSITA to serve the same function as disclosed in the '370 Patent.

[303] At para 205, he summarizes his opinion that the various limitations on the concentration of chemical species in the same claims are consistent with the information available to the POSITA before September 2006 and that these limitations would not be surprising to the POSITA.

[304] With respect to the physicochemical parameters, i.e., the pH range and osmolality values, Dr Kent indicates at para 207 that the sole difference between the subject matter of Claims 1-15 and 28-34 and the state of the art is the specification of the upper limits for certain components, for example, less than 15 mM. He adds that a POSITA would find these limitations consistent with teachings of the prior art and that the restrictions in the claims of the '370 were self-evident and obvious.

[305] Dr Kent notes at para 209 that when formulating an ophthalmic composition, a goal of the POSITA is to use the lowest concentration of components while not compromising the required properties of the composition. He adds that the POSITA would want to keep the concentration of buffering anions as low as possible to avoid the pH in the composition causing

discomfort. The POSITA would also have been motivated to keep the concentration of multivalent cations low.

[306] Dr Kent clarifies at para 210 that in the event he is incorrect in this view, these limitations would have been readily determinable as part of routine regular formation development.

[307] At para 212, Dr Kent indicates that as of September 21, 2006, it would have been routine for a POSITA to screen several formulations to gather information about what components have a negative impact on the antimicrobial activity of the zinc ions.

[308] Overall, he expresses the opinion that any differences that exist between the prior art and the subject matter of claims 1-15 and 28-34 would have been self-evident and/or readily ascertainable by the POSITA.

[309] Dr Kent focusses on claims 10 and 13 at paragraphs 214-222 of his affidavit and restates that both claims would have been obvious or self-evident. He notes that Claim 13 pertains to an ophthalmic solution containing specific components (as set out in the claim). He indicates that as of September 2006, the POSITA knew that travoprost could be used in ophthalmic compositions. In addition, Xia and Kiyobayashi disclosed ophthalmic compositions containing zinc in the concentration range of the claim (0.04-0.4). Kiyobayashi disclosed compositions containing zinc ions and borates, propylene glycol and sorbitol. The first Chowhan patent taught the suitable amounts of borate and propylene glycol or sorbitol. With respect to limits on anionic species (of less than 15 mM), and particularly buffering anions, Dr Kent states at para 218 that the POSITA

would know to minimize the concentration so as not to affect the eye's capacity to regulate pH after application to the eye.

[310] At para 219, Dr Kent adds that Xia, the first Chowhan patent, and the product monograph for Travatan, plus the common general knowledge included teachings to keep the pH within the claimed range.

[311] With respect to Claim 10, Dr Kent indicates that the only difference between Claim 10 and what was disclosed in Kiyobayashi is the inclusion of travoprost. Travoprost was well known by September 2006. Dr Kent expresses the opinion that it would have been self-evident that travoprost could be added to the compositions disclosed in Kiyobayashi. Dr Kent indicates at para 221 what the art disclosed regarding the claims upon which Claim 10 depends and concludes that both Claims 10 and 13 were self-evident to a POSITA.

E. *The Allegations of Obviousness Are Justified*

[312] Based on the submissions of the parties and the evidence of the experts, the application of the *Plavix* test leads me to the conclusion that Alcon has not established that Apotex's allegations that the '370 was obvious are not justified.

[313] The *Plavix* test directs the Court to first identify the POSITA, the common general knowledge and the inventive concept of the claim.

[314] The POSITA has been identified above at para 111. The common general knowledge has been described by both Alcon's expert, Dr Loftsson, and Apotex's experts, Dr Miller and Dr Kent. There is substantial agreement about the common general knowledge but there is some disagreement about the teachings of the prior art, particularly the teachings of Xia and Kiyobayashi regarding anionic species limits.

[315] Dr Miller's evidence provides an overview of the common general knowledge and state of the art, which I accept.

[316] Alcon argues that there are at least four inventive concepts including the solution to the particulate problem. Apotex argues that the inventive concept is more general and does not include the enhancements or "bells and whistles" and, in particular, does not include limits on anionic species. I do not accept either of these positions.

[317] I have found the inventive concept to be a (self-preserved) multi-dose ophthalmic composition or formulation containing travoprost that does not include BAK and which uses a non-conventional preservative system that includes low levels of zinc chloride, a borate/polyol complex (or propylene glycol and sorbitol) and low levels (less than 15 mM) of anionic species and specific osmolality values.

[318] The differences between the "state of the art" and the inventive concept and whether this invention was obvious to try are the focus of the obviousness analysis.

[319] The expert evidence is essential to assist the Court in this analysis. However, this proceeding has highlighted the limitations of written affidavits and transcripts of cross-examinations of the expert affiants as the only evidence.

[320] Counsel for Apotex, through their cross-examination, succeeded in having Dr Loftsson admit that he did not understand the law of obviousness, and even more troubling, that he tends to forget things he is told.

[321] While Dr Loftsson is no doubt an accomplished scientist and he responded to all questions thoroughly and candidly, his evidence on the issue of whether the invention is obvious was undermined on cross-examination.

[322] Specific questions were put to him that required him to either agree or disagree. Counsel for Apotex took apart his evidence on several key points that are essential to support Alcon's position. Although some words appear to have been put in his mouth, calling for a yes or no answer, his evidence was undermined. For example, Apotex suggested to him that the further enhancements noted in the Patent were not essential features or the inventive concept but rather "bells and whistles". He agreed.

[323] Cross-examination revealed that Dr Loftsson appears to have assessed obviousness from his own perspective as a potential POSITA rather than from the broader criteria or qualifications of the team of experts which makes up the POSITA. He acknowledged that he had not been instructed how to read the Patent, he did not understand the concept of obviousness in the

Canadian law, he used September 2007 as the relevant date for his obviousness inquiry, and he considered art that existed after that date.

[324] Dr Loftsson also indicated that he was advised not to consider Systane Free in assessing obviousness, although it had been referred to in the NOA.

[325] Alcon acknowledges that Dr Loftsson was confused by the law of obviousness, but submits that he was clear about the science. Alcon also submits that Dr Loftsson may have referred to the art after September 2006 but his opinion on obviousness is not based on this post-2006 art.

[326] I cannot determine what art Dr Loftsson relied on as his answers on cross-examination indicate that he conducted additional research and found many articles, several of which he read. The dates of the articles he relied on or may have been influenced by, in some way, in reaching his opinion have not been clearly noted in his evidence. Several of the footnotes refer to post-2006 publications some of which are very recent publications.

[327] Alcon also asks the Court to come to an independent conclusion whether the invention is obvious.

[328] I have considered all the evidence with respect to the differences between the state of the art and the inventive concept. I have carefully read Dr Loftsson's evidence, but given the problems with it, I have relied more heavily on the evidence of Dr Miller and Dr Kent.

[329] The *difference between the state of the art and the inventive concept* simply put is the replacement of the preservative system previously used in Travatan which used BAK with the BAK free preservative system of the current invention. Dr Miller and Dr Kent note that the key difference in the state of the art and the invention is the specification of the upper limits for some components and the difference would be self-evident.

[330] The expert evidence of Dr Miller and Dr Kent which I have put more weight on relies on the mosaic of the prior art, as it should in an obviousness inquiry. It reveals that the POSITA knew that travoprost could be used in ophthalmic compositions; Xia and Kiyobayashi disclosed ophthalmic compositions containing zinc in the concentration range of the claim (0.04 -0.4 mM); Kiyobayashi disclosed compositions containing zinc ions and borates, propylene glycol and sorbitol; and Chowhan #1 taught the appropriate amounts of borate and propylene glycol or sorbitol; Xia, the first Chowhan patent, and the product monograph for Travatan, plus the common general knowledge included teachings to keep the pH within the claimed range.

[331] The Systane Free preservative system was also known and that system includes the same components or ingredients as Claim 13. As Dr Miller indicates, the composition of Systane Free was disclosed and also could have been reverse engineered. The composition details show that zinc chloride, boric acid, propylene glycol and sorbitol had already been successfully formulated together.

[332] Dr Kent's evidence is that the POSITA, knowing the components of Systane Free, would recognize that the zinc ions derived from zinc chloride at a concentration equivalent to 0.11 mM

was the primary preservative. The POSITA would also understand, based on the Chowhan patents, that borate-polyol complexes would exhibit antimicrobial activity to supplement that provided by zinc ions.

[333] The evidence regarding the teaching of the limits on anionic species is more carefully worded by the experts.

[334] Dr Miller indicates that the POSITA would have been motivated to keep the concentrations of anionic species as low as possible based on the teachings of Xia and Chowhan.

[335] Dr Kent acknowledges that the specific limit on anionic species of less than 15 mM was not disclosed in the prior art but the POSITA would know to minimize the concentration so as not to affect the eye's capacity to regulate pH after application to the eye. Dr Kent notes that the Xia application does not include an explicit discussion of the amount of anionic species in the composition but the compositions described in Xia include those with a concentration of anionic species of less than 15 mM. He also acknowledges that Kiyobayashi disclosed compositions containing anionic species, buffering anions, multivalent cations or ionized salts but did not include an explicit discussion of the levels for these components. He adds that Kiyobayashi included "guidance against using amounts of excipients that would conflict with the preservation characteristics of the compositions."

[336] Dr Kent states that the sole difference between the subject matter of claims at issue and the state of the art is the specification of the upper limits for certain components, "e.g. less than

15 mM", which refers to anionic species. His opinion is that a POSITA would find these limitations consistent with teachings of the prior art and that the restrictions in the claims of the '370 were self-evident and obvious.

[337] Dr Kent and Dr Miller both indicated that when formulating an ophthalmic composition, a goal of the POSITA is to use the lowest concentration of components while not compromising the required properties of the composition and would want to keep the concentration of buffering anions as low as possible.

[338] Dr Kent also indicates that these limitations would have been determinable as part of routine regular formulation development.

[339] The evidence of Dr Miller and Dr Kent, which I accept, is that the POSITA would have a fair or reasonable expectation of success that the preservative system of Systane Free or the very similar preservative system of the present invention would work and that only routine experiments would be required to make necessary adjustments. It was more than "worth a try", even without specific teachings on the specific limits of anionic species. It would have been self-evident that what was being tried would work as a non-conventional preservative system for an ophthalmic formulation.

[340] Although Systane Free is only one piece of the prior art, it was very relevant prior art. Dr Loftsson did not address the teachings of Systane Free at Alcon's instruction. Alcon attempts to downplay Systane Free as a precursor to the invention, although Alcon itself described the

invention as an *extension* of the preservative system used in Systane Free. This is curious because Alcon now argues that Systane Free is a different system and the POSITA would recognize this.

[341] However, the components of the preservative system in Systane Free are the same as the preservative system in Claim 13. Although refinements to the levels of other aspects of the composition or formulations would be needed, Systane Free cannot be characterised as a different system. Dr Miller and Dr Kent both agreed that Systane Free taught the combined use of zinc chloride, boric acid and propylene glycol and sorbitol.

[342] Apotex provides a chart comparing the components of Travatan, Systane Free and Claim 13 of the '370. Even to the layman's eye, the components or ingredients of the preservative system are the same. The differences between the preservative system in Systane Free and Claim 13 relate to the concentration of zinc chloride. A limit on the anionic species is provided for Claim 13 but none for Systane Free.

[343] In addition to its submissions that the invention was obvious, Apotex reiterates that Alcon must establish on a balance of probabilities that its allegation is not justified. Apotex submits that Alcon has not met its burden even if the evidence is evenly balanced.

[344] Whether the prior art did or did not disclose the specific levels of anionic species is not conclusive. Because a low level of anionic species (of less than 15 mM) is part of the inventive concept, the issue is whether this was disclosed in the mosaic of the prior art.

[345] Apotex's experts agree that this was taught generally in Xia and Kiyobayashi, but acknowledge that the specific limits were not taught. Apotex's experts add that the common general knowledge is to keep all concentrations low and that a POSITA, relying on their skills and the common general knowledge would know this and would do so. In addition, only routine experimentation would be needed to reach the invention. The prior art plus the common general knowledge taught that low levels were needed and the routine experimentation using the skills of the POSITA would result in the invention.

[346] Alcon's submission that it was not obvious to try, that there was no reasonable expectation of success and that considerable experimentation was required, is not supported by the evidence of Dr Miller and Dr Kent.

[347] As a result, I find that it was more or less self-evident that the invention would work. Although it was not guaranteed, there was a reasonable expectation of success and it was far more than "worth a try".

[348] In addition, all the experts agreed that there was *motivation* in the prior art to remove BAK from ophthalmic formulations due to the side effects associated with BAK. Dr Miller noted that there were ample precedents in the prior art to motivate the POSITA.

[349] With respect to the amount of *effort* required to achieve the invention, Alcon's own expert, Dr Loftsson, agreed that the laboratory work to prepare and test new formulations of

travoprost and its preservation was not arduous. He noted that Preservative Efficacy Testing [PET] would be time consuming but added that this was largely automated.

[350] In conclusion, I find that Alcon has not met its burden; it has not established that Apotex's allegation of obviousness for Claims 10 and 13 is not justified.

XIV. UTILITY

[351] In the present case, Alcon and Apotex have different views on the promised utility of the '370. Alcon submits that the utility is simply to be useful and to meet the USP preservative efficacy testing standards or to provide an alternative choice and that this utility was soundly predicted.

[352] Apotex asserts two promises of utility: the first, which was set out in the NOA refers to a promise of minimization or reduction of side effects; and, the second, which was raised after the NOA, refers to a promise of an acceptable formulation, without particulate matter. I have found that Apotex's second or revised assertion of promised utility is beyond the scope of the NOA and it has not been considered. Nevertheless, the arguments advanced by Apotex are summarized below.

[353] Apotex argues that the promised utility of minimization or elimination of side effects was not soundly predicted. Apotex also submits that the revised promise of utility was not soundly predicted.

A. *Jurisprudence / Principles Regarding the Promise of the Patent*

[354] The Court of Appeal has confirmed that there is no obligation on the part of a patentee to disclose the utility of the invention in the patent. In such cases, a "mere scintilla" of utility will be sufficient (*Eli Lilly Canada Inc v Novopharm Limited*, 2010 FCA 197 at paras 74-76 (*Olanzapine*); *Mylan Pharmaceuticals ULC v AstraZeneca Canada Inc*, 2012 FCA 109, [2012] FCJ No 422 [*Anastrozole*] at paras 32-33). However, where there is a promise of utility, which should be explicit, the patentee will be held to the promised utility (*Olanzapine*). As noted by the Federal Court of Appeal in *Apotex Inc v Sanofi-Aventis*, 2013 FCA 186, [2013] FCJ No 856, leave to appeal to SCC granted, 35562 (October 1, 2013) at para 50, the first step is to construe the patent and determine the standard against which the utility will be measured. The Court of Appeal added, "This requires the Court to construe the patent to determine if a person skilled in the art would understand it to contain an explicit promise that the invention will achieve a specific result. If so, the inventor will be held to that promise. If there is no explicit promise of a specific result, then a mere scintilla of utility will do."

[355] The Court of Appeal also cautioned against promising more than is required and bearing the consequences of a "self-inflicted wound" if that promise is not met, but emphasized that the Courts "should not strive to find ways to defeat otherwise valid patents" (para 54).

[356] In determining what the promised utility is, the Court must first look to the claims but with a view to the patent as a whole. Not every statement of advantage in the specification rises to the level of promised utility. The construction of the claims, as noted above, is the first step and should not be results-oriented.

[357] In *Anastrozole*, above the Federal Court of Appeal agreed with the trial judge's conclusion that there was no promise to reduce side effects. Based on an examination of the patent, a sentence setting out the object of the invention, unlike the express claims of the patent, was "no more than a forward-looking aim of the invention" (para 33). The Court also noted at para 30 that a promise to this effect "would be entirely gratuitous, and could only provide competitors with another basis for attacking its validity."

[358] In the present case, Alcon argues that a promise of reduced side effects would be "gratuitous".

[359] In *Fournier Pharma Inc v Canada (Minister of Health)*, 2012 FC 741, [2012] FCJ No 901 at para 126, Justice Zinn noted that where the claims clearly set out the promise, (i.e. the claimed utility), other statements "should be presumed to be a mere statement of advantage unless the inventor clearly and unequivocally states that it is part of the promised utility."

[360] Justice Zinn added at para 127 that the focus should be on the claims because an inventor need not "claim a monopoly on everything new, ingenious, and useful" that is disclosed. Justice Zinn cautioned that where the claims are unambiguous in stating the promise "then the disclosure should not be examined microscopically to find additional promises that are outside the scope of the inventor's claimed monopoly."

[361] In *Pfizer Canada Inc v Mylan Pharmaceuticals ULC*, 2014 FC 38, [2014] FCJ No 126, Justice Harrington confirmed the principle that the claims take precedence when determining

what is promised. Although the disclosure may lead to an understanding of what is meant by a word in the claims it does not contract or enlarge the scope of the claims.

[362] Justice Harrington relied on *Sanofi-Aventis v Apotex Inc*, 2013 FCA 186, [2013] FCJ No 856 at para 67, where the Court of Appeal noted the distinction between the potential use of an invention and an explicit promise to achieve a specific result and cited with approval the view of this Court in *AstraZeneca Canada Inc v Mylan Pharmaceuticals ULC*, 2011 FC 1023, [2011] FCJ No 1262 at para 139 "that not all statements of advantage in a patent rise to the level of a promise. A goal is not necessarily a promise." Justice Harrington found that there was no mention of reduced side effects in the claims and this was not the promised utility.

B. *Alcon's position on the Promised Utility*

[363] Alcon submits that the utility disclosed by the '370 Patent is only the provision of self-preserved ophthalmic formulations that pass USP preservative effectiveness/efficacy testing. The invention provides a useful alternative preservative system.

[364] Alcon notes that the goal was to develop a multi-dose product that avoids the use of BAK. Alcon relies on the evidence of Dr Loftsson, who acknowledged that a POSITA may expect this result (of reduced side effects) but it was not promised and that such a promise would require clinical investigation. Alcon also notes that a goal is not a promise.

[365] Alcon argues that Apotex has incorrectly elevated the promised utility of the '370 Patent, by suggesting that the "claimed ophthalmic compositions/solutions exhibit antimicrobial activity

("self-preserved") with concomitant minimization or elimination of toxicological effects (harmful effects on the cornea)".

[366] Alcon submits that such a promise cannot be implied and that there is no explicit promise in the '370. The Patent does not include any comparative testing of formulations covered by the claims with formulations containing BAK, toxicity testing, or any statement that formulations of the invention would be less toxic than formulations containing BAK.

[367] Alcon also notes that the '370 is consistent with the prior art, particularly Xia and Kiyobayashi, who also attempted to develop BAK-free formulations, but did not provide comparative toxicology testing.

[368] Alcon further submits that the Court should endeavour to support a really useful invention (*Consolboard Inc v MacMillan Bloedel (Sask) Ltd*, [1981] 1 SCR 504 [*Consolboard*] noting that the self-preserved formulation without BAK provides a useful alternative to the public.

[369] As noted above in the discussion of the NOA, Alcon argues that Apotex cannot now assert that there are two promises of utility; the promise of reduced side effects which Apotex originally set out in its NOA, and a revised or additional promise, of an "acceptable ophthalmic formulation", which Apotex only raised after cross examination of the experts.

[370] Alcon submits that, in any event, Claim 13 is limited to solutions that, by their nature, do not have particulate matter because everything is dissolved. Apotex acknowledged in its NOA that Claim 13 was a solution where "all components are dissolved" and it cannot take a different position now.

[371] Moreover, Alcon argues that the Patent teaches how to avoid formation of particulate matter. In addition, Claim 10 is for compositions and particulate matter is not an issue at all.

C. *Apotex's position on the Promised Utility*

[372] Apotex submits that the promised utility should be construed within the context of the Patent as a whole and through the eyes of a POSITA, with commercial realities in mind which would reveal the patentee's intent.

[373] Apotex notes that the POSITA would have understood that ophthalmic compositions that are toxic to the eye would not be appropriate for patient use. The '370 refers to the "need for a means of enhancing the activity of anti-microbial agents so that very low concentrations of the agents can be utilized without increasing the potential for toxicological effects […]". The invention is stated to be for the control of intraocular pressure and the POSITA would know that this requires chronic administration.

[374] Apotex submits, therefore, that the promised utility is the provision of ophthalmic formulations that reduce or eliminate the side effects caused by traditional preservatives such as BAK, including harmful effects on the cornea, when the compositions are used to control

intraocular pressure and treat glaucoma on a chronic basis. In its NOA Apotex asserts the reduced side effects promise as the promised utility.

[375] As noted above in the discussion of the NOA, Apotex now asserts a revised or new promise of utility based on statements in the '370 that the ophthalmic compositions "have sufficient antimicrobial activity to satisfy the preservation efficacy requirements of the USP and analogous guidelines" and that "particle matter formation is not acceptable for ophthalmic formulation."

[376] Apotex also notes that Alcon has asserted that overcoming the particulate problem is part of the inventive concept. But, with respect to the promised utility, Alcon argues that a promise of an acceptable formulation (i.e., with no particulate matter) would be "gratuitous". Apotex submits that having defended the inventiveness of the '370 on the basis of overcoming the particulate problem, Alcon must also accept that the promised utility includes compositions free of particulate matter.

[377] Apotex maintains that its first position remains that overcoming the particulate problem is not part of the inventive concept. However, Apotex submits that, due to Alcon's position on the inventive concept, Alcon must concede that the promised utility includes that there will be no formation of unacceptable particulate matter; i.e. that the formulation will be acceptable.

[378] Apotex acknowledges that the NOA did not assert that the promise was for an "acceptable", meaning free of particulate matter, formulation, but argues that Alcon cannot read the patent one way to support its inventiveness and another to meet the utility attacks.

[379] Apotex argues that the promised utility of simple usefulness asserted by Alcon bears no resemblance to Alcon's proposed inventive concept. Apotex points to *Olanzapine* at para 78, which dealt with a selection patent, for the more general proposition that, "if the advantage is not promised, the patentee will not be able to rely on the advantage to support the patent's validity".

[380] Apotex characterizes as incoherent Alcon's argument that there is no particulate problem or that it has been addressed because Claim 13, which refers to "solutions", is understood to be a solution where all components are dissolved and, as such, would exclude particulate matter.

[381] Apotex also disputes Alcon's argument that the '370 teaches how to avoid the particulate problem by adjusting the pH. Apotex argues that the evidence is just the opposite - while Alcon knew how to avoid the problem, by reducing the pH to 5.7 which is the level used in the commercial product, Travatan Z, it failed to disclose the amount of HSA formed in its own testing and elected to claim solutions with a pH of up to 5.9, leaving the POSITA "in the dark" about how to arrive at solutions without particulate matter. Having failed to disclose this information in the Patent, Alcon cannot meet the test for sound prediction.

D. *What do the Expert's Say?*

(1) Dr Loftsson

[382] Dr Loftsson disagrees with Apotex's view of the utility that the invention promised both a self-preserved formulation and minimization or elimination of toxicological effects on the cornea.

[383] At para 239 of his affidavit, Dr Loftsson notes that the inventors removed BAK from their eye drops and replaced it with a complex preservative system that contains low concentrations of zinc. At para 240, Dr Loftsson states:

> […] conventional preservatives (such as BAK) have been widely discussed in the literature as having potentially toxic effects on the cornea. Eliminating such preservatives while maintaining preservation is a desirable objective, one that the inventors achieved. The inventors are not promising that their preservations system will minimize or eliminate toxicological effects. While a skilled person may reasonably expect such an outcome based on the elimination of conventional preservatives, evidence for such a conclusion would require substantial clinical investigation, well beyond the clinical work necessary to obtain regulatory approval.

[384] Dr Loftsson concludes at para 242 that the utility is the provision of self-preserved ophthalmic formulations.

[385] On cross-examination, at Q 385-388, Dr Loftsson agrees that the Patent is directed to the improvement of preservative systems containing zinc ions and further agrees that the focus was not simply delivering a preservative system containing zinc, but an improved system.

(2) Dr Miller

[386] Dr Miller indicates at para 49 of his affidavit that a POSITA would understand that the goal of the invention was "to obtain an aqueous pharmaceutical composition having a suitable level of preservative effectiveness for a multi-dose format".

[387] Dr Miller also provides comments on Dr Loftsson's affidavit. He agrees with Dr Loftsson that one aspect of the utility of the '370 is the provision of self-preserved ophthalmic formulations, but he disagrees with Dr Loftsson's opinion that the utility does not include the elimination or minimization of the toxicological effects on the cornea. Dr Miller notes that the POSITA would understand that the inventor was moving away from traditional preservatives toward preservative strategies that were less toxic and he notes that the '370 specifically states that it was directed at compositions that did not contain the conventional preservatives which could cause corneal complications.

[388] Dr Miller expresses the opinion at para 278-283 that the POSITA would understand that the intent of the inventors was to prepare ophthalmic compositions that would minimize or eliminate the toxicological effects of BAK because the compositions replace BAK with zinc ions that would have been expected to avoid these effects.

[389] Dr Miller disagrees with the statement at para 240 of Dr Loftsson's affidavit and notes that the "skilled person would have understood that ophthalmic compositions that are toxic to the eye would not be appropriate for patient use". He reiterates at para 285-287 that the skilled person would have understood the intent of the inventors was to minimize or eliminate the

toxicological effects of BAK by replacing it with zinc ions and that the skilled person would have understood that standard toxicological and clinical studies are required to be performed in order to obtain regulatory approval.

[390] On cross-examination, at Q 254 and Q 261, Dr Miller agrees that the goal of the inventors is to provide a multi-dose product that avoids using BAC and to avoid the toxicities associated with conventional preservatives.

[391] At Q 271, Dr Miller agrees with a statement put to him by Counsel for Alcon that at line 25, page 4 of the Patent the inventors are stating that the skilled person would understand that the invention related to multi-dose products that do not require a conventional preservative and yet are preserved from microbial contamination.

[392] Dr Miller agrees but notes that there is no definition of "conventional" provided.

[393] At Q 291, Dr Miller agrees that there is no explicit statement in the '370 that the formulations of the invention would be less toxic than BAK. However, Dr Miller goes on to indicate that a POSITA would understand that "what is inherently taught is that the invention would be less toxic compared to other ophthalmic compositions that do contain other preservatives such as BAC."

[394] Dr Miller indicates at Q 292 that this opinion is based on the teaching that BAK is known to be toxic and BAK is "called out as an example of a preservative within the 370 Patent that can be toxic to the cornea."

[395] Although Dr Miller indicates that he has objections to the use of the term "self preserved" in the Patent, he responds to Q 293 regarding how the POSITA would understand the inventors' goal to eliminate BAK and by "limiting" BAK be less toxic to the ocular surface and indicates that the POSITA would understand what is being taught. He indicates that the invention is a multi-dose composition and is eliminating or reducing the toxic effect, for example, from BAK.

(3) Dr Kent

[396] Dr Kent sets out his detailed opinion on utility at para 223-224 noting that the '370 Patent says that the use of BAK results in potential harmful effects on the cornea and that the use of BAK should be avoided. The POSITA would, therefore, understand that "the utility of the claimed compositions of the 370 Patent is that they will exhibit antimicrobial activity (the compositions are self-preserved) while reducing or eliminating the side effects caused by BAK (the harmful effects on the cornea) when the compositions are used to control intraocular pressure to treat glaucoma."

[397] Dr Kent also provides comments on Dr Loftsson's affidavit. At para 248, Dr Kent notes that the provision of self-preserved ophthalmic formulations is only one part of the utility and that Dr Loftsson "leaves out an important aspect - the avoidance of deleterious effects on the cornea". Dr Kent refers to the disclosure of the '370 and expresses the opinion that the POSITA

would have recognized that the inventors were proposing compositions that "sidestep the deleterious corneal effects of BAK by replacing it with zinc ions".

[398] On cross-examination, at Q 320-321, Dr Kent agrees that the invention was directed to self-preserved formulations that do not require a conventional antimicrobial agent and that the goal was to provide a multi-dose formulation that avoids using BAK or similar compounds.

[399] He also agrees that there is no discussion of toxicity relative to BAK in the first paragraphs of the Patent.

[400] He also agrees with questions put to him that BAK was known to cause side effects and the inventors sought to eliminate BAK and the associated side effects.

[401] At Q 331, Dr Kent notes that there were known side effects from BAK but not to the extent that products containing BAK were withdrawn from the market. He agrees that if BAK is eliminated the side effects of BAK would be eliminated "if you have a non-preserved product", explaining that each preservative system needs to stand on its own (at Q 334).

[402] Later in the cross examination, at Q 443-450, Dr Kent is asked about several references in the Patent, particularly in the Summary of Invention, and whether there is any promise of reducing toxicity relative to BAK. He agrees that there is no promise.

[403] At Q 450, Counsel for Alcon directs Dr Kent to page 6 of the Patent where it states that the invention is directed to the provision of aqueous ophthalmic solutions that are effective in preventing antimicrobial contamination in the absence of conventional antimicrobial preservatives. Dr Kent agrees that to have a self-preserved formulation that does not contain BAK is useful and provides another choice.

[404] In response to Q 455, Dr Kent agrees that the '370 does not include any comparative testing of formulations with or without BAK, in relation to toxicity.

[405] However at Q 462, Dr Kent does not fully agree that there is no promise that the invention would not be less toxic than conventional preservatives. He indicates that "some of the language in the patent that there is a promise that it is going to be better […] obviously, it is going to be a different preservative, but on top of that, there is this thing that -- you know, it is not just going to be another preservative, it is going to be one that going to be better than what is there, and better than relative to toxicity, otherwise known as ocular hyperemia […]."

[406] In response to Q 463 he agrees with the proposition put to him that the promise was not express but "implied".

E. *The Promised Utility*

[407] In determining the promised utility, the claims are the starting point. Where the promise cannot be discerned from the claims the disclosure will inform the meaning of the claims, but cannot enlarge or contract what is stated in the claims.

[408] The promised utility must be explicit. If there is no explicit promise, there is no need to hunt for a promise elsewhere because not every patent includes such a promise.

[409] As noted above in the discussion of the construction of the claims, there is no mention of any reduction in side effects in Claims 10 or 13 (or in any of the claims). Moreover, there is no mention of any particular use in Claims 10 or 13. Of the 35 claims of the Patent, only four claims set out a proposed use (Claims 11, 12, 14 and 15) which is for the control of intraocular pressure. While the specification indicates that the invention is directed at ophthalmic compositions which are applied to the eye, and includes a specific statement at page 6b that the "present invention further provides a use of travoprost in a composition or solution of the invention for control of intraocular pressure", a proposed use is not set out in Claims 10 or 13.

[410] Only two of the 35 claims (Claim 16 and 35) refer to any enhancement and this refers to antimicrobial activity, not side effects.

[411] The Court must consider how the POSITA would interpret the promise of the Patent.

[412] Dr Loftsson's evidence that a promise of reduced side effects would be a reasonable expectation for a POSITA is quite candid. However, Dr Loftsson is of the opinion that this is not the promise.

[413] Dr Miller's evidence is that the POSITA would understand that the intent of the inventors is to minimize or eliminate the side effects of BAK. Dr Kent also indicates that the utility

includes reducing or eliminating side effects and that the POSITA would recognize that the inventors are aiming to "sidestep" the effects of BAK. Both Dr Miller and Dr Kent disagree with Dr Loftsson that the utility is only that of a self-preserved ophthalmic composition. However, on cross-examination they both acknowledge that there is no explicit promise.

[414] Dr Miller agrees that this is a goal of the inventors and it is inherently taught, but there is no explicit statement. Dr Kent agrees that the inventors sought to eliminate the BAK and its associated side effects, but also agrees there was no promise of reducing toxicity relative to BAK and that the promise is implied.

[415] The expert evidence all seems to land on the view that while there may be a reasonable expectation of a promise to eliminate or minimize the side effects associated with BAK, given the goal of the inventors to replace BAK, there is no such explicit promise and any notion of a promise is implied or inherently taught.

[416] Moreover, the wording of the claims is clear. There is no promise of reduced side effects in Claims 10 or 13 or in the Patent. There is no promise of any particular use in Claims 10 or 13. While a promise may be expected given the need to avoid BAK and its side effects, and while some of the experts would imply such a promise, this cannot be read into the claims.

[417] The promised utility is simply to provide a self-preserved ophthalmic formulation without BAK that passes the USP preservative efficacy testing, and provides a useful alternative preservative system: i.e. another choice for ophthalmic formulations.

[418] The question to be determined next is whether the Patent lives up to its promised utility.

F. *Jurisprudence/Principles Regarding Demonstrated and Sound Prediction of Utility*

[419] In *Apotex Inc v Pfizer Canada Inc*, 2011 FCA 236, [2011] FCJ No 1234 [*Pfizer*] at para 30 the Court of Appeal established that the general principle is that, as of the date of the filing, a patent must disclose an actually achieved result (i.e. it does what it claims) or a basis for sound prediction (i.e., that it is likely to do what it claims). The Court of Appeal added that where the demonstrated utility is not set out in the disclosure, the disclosure must refer to a study demonstrating that the patent does what it promises to do.

[420] In other words, where utility is not demonstrated, it must be soundly predicted.

[421] The Court of Appeal in *Pfizer* explained the purpose of the doctrine of sound prediction at para 33:

> [33] The doctrine of sound prediction seeks to balance two competing public interests: the desirable early disclosure of new and useful inventions, even though their utility has not been fully verified by tests, and the need to ensure that patent rights are not granted in exchange for misinformation (*Sanofi*, at paragraph 105; *Wellcome AZT*, at paragraph 66). Thus, if a patentee can articulate a sound prediction as to the utility of his invention, he should be entitled to base a claim on it. And although patents shall not be granted in exchange for misinformation, mere speculation or lucky guesses, a sound prediction does not amount to certainty (*Wellcome AZT*, at paragraph 69; *Monsanto Co. v. Canada (Commissioner of Patents)*, [1979] 2 S.C.R. 1108, at page 8).

[422] The doctrine of sound prediction of utility was established by the Supreme Court of Canada in *Apotex Inc v Wellcome Foundation Ltd*, 2002 SCC 77, [2002] SCJ No 78 [*AZT*] at

para 70. There are three elements: there must be a factual basis for the prediction; there must be an articulable and sound line of reasoning from which the desired result can be inferred from the factual basis; and, there must be proper disclosure and it is normally sufficient if the specification provides a full, clear and exact description of the nature of the invention and the manner in which it can be practiced.

[423] The third element -- proper disclosure -- has been the subject of a great deal of jurisprudence. That jurisprudence has established that the disclosure should be in the Patent. In *Eli Lilly Canada Inc v Apotex Inc*, 2008 FC 142, [2008] FCJ No 171 at para 164, aff'd 2009 FCA 97, Justice Hughes highlighted that "The public should not be left to scour the world's publications in the hope of finding something more to supplement or complete a patent disclosure. As the Supreme Court said at paragraph 70, the *quid pro quo* offered in exchange for the monopoly is disclosure. It must be in the patent."

[424] The Court of Appeal agreed (2009 FCA 97 at para 18) and emphasized the importance of the disclosure obligation, explaining that in *AZT*, the Supreme Court of Canada established that "[…] the patent must provide a disclosure such that a person skilled in the art, given that disclosure, could have as the inventors did, soundly predicted that the invention would work once reduced to practice."

G. *Alcon's Position on Demonstrated or Soundly Predicted Utility*

[425] Given Alcon's position that the utility is simply to provide a self preserved ophthalmic solution that passes the USP preservative efficacy testing, Alcon submits that the utility has been met and relies on Dr Loftsson's evidence in support.

[426] I note that Alcon acknowledges that if the promised utility had been found to include reducing the side effects, Alcon has no evidence to demonstrate such utility because it did not conduct any testing for toxicity. However, Alcon argues that there is a sound prediction of reduced side effects. Alcon points to the expert evidence which indicates that: the side effects associated with BAK can be avoided by eliminating the excipient from the formulation and replacing it; zinc, propylene glycol, sorbitol and borate are less toxic than BAK; and, boric acid is a commonly used excipient. The POSITA would expect that the formulations would avoid the side effects associated with BAK. Alcon argues that a factual basis and a sound line of reasoning existed, based on the information and science available at the time and were disclosed.

H. *Apotex's Position on Demonstrated or Soundly Predicted utility*

[427] Apotex focusses its argument that there was no demonstrated or soundly predicted utility on the two promises of utility which it asserts, neither of which has been found to be the promised utility.

[428] Apotex submits that the promise of reduced side effects was not soundly predicted because there was no factual basis for such a prediction; there was no testing of side effects.

[429] Apotex also submits that the promise of an acceptable ophthalmic formulation was not soundly predicted. Based on the testing disclosed in the Patent, the POSITA would expect particulate matter to form and the formulation would fail PET. Therefore, there could be no sound prediction of an acceptable formulation.

[430] Apotex advances detailed arguments with respect to the lack of sound prediction for the revised promise of utility of an acceptable formulation and focusses on the lack of disclosure by Alcon of their stability testing following the discovery of the particulate matter problem. If the Court had found the promise of an acceptable (i.e. particulate free) formulation to be the promised utility, the lack of disclosure could have been fatal to the sound prediction of this utility.

[431] I also note that Apotex argued that the POSITA would know how to resolve the particulate problem, so it would be "acceptable". However, this issue need not be addressed because this is not the promised utility and Apotex's assertion is beyond the scope of the NOA.

[432] Apotex did not advance arguments regarding the sound prediction of the utility of the invention as a self-preserved ophthalmic formulation without BAK that passes the USP preservative efficacy testing and provides a useful alternative preservative system: i.e., another choice for ophthalmic formulations.

I. *What do the Experts Say about Demonstrated or Sound Prediction of Utility?*

[433] Dr Loftsson provides his opinion at para 294 of his affidavit on the demonstrated or soundly predicted utility based on his perspective that the utility was simply the provision of a self-preserved ophthalmic solution.

[434] Dr Loftsson refers to the chemical composition described by Claim 13, the disclosed characteristics of zinc based preservative systems, the test results provided in the '370 for preservative systems, the examples directed to the combination of components, the anionic species limit and the zinc chloride concentration. At para 310 he states his overall conclusion:

> The inventors provided examples of formulations that both passed and failed PET, including formulations that are within or very close to the elements of claim 13. The inventors tested formulations with differing pH and zinc concentrations, and on either side of the 15 mM limit on anionic species. The 370 patent described the inventors' reasoning on how zinc functions as an antimicrobial and why propylene glycol is especially preferred. The inventors also explained the various ionic interactions between zinc and other species in solution.

[435] Dr Loftsson concludes at para 311 that he believes the '370 "provides facts and reasoning that support a reasonable scientific hypothesis for proposition that the claim 13 formulations would be self preserved and would pass USP PET ".

[436] He expresses the same opinion at para 312-316 with respect to Claim 10, based on two alternative interpretations.

[437] Dr Kent expresses the opinion that the promised utility of the ‘370, which in his view includes the promise of reducing or eliminating side effects caused by BAK, had not been demonstrated.

[438] He also expresses the opinion that the inventors did not have a factual basis and a sound line of reasoning in order to soundly predict this promised utility.

J. *The promised utility was soundly predicted*

[439] Having found that the promised utility is simply to provide a self-preserved ophthalmic formulation without BAK that passes the USP preservative efficacy testing, and provides a useful alternative preservative system, i.e., another choice for ophthalmic formulations, I find that this utility was soundly predicted.

[440] Apotex did not address the issue of demonstrated or soundly predicted utility from the perspective of the simple utility.

[441] Dr Loftsson’s evidence on sound prediction of this utility was not challenged in any way.

[442] The three part test set out in *AZT*, above, calls for a factual basis for the prediction; an articulable and sound line of reasoning from which the result can be inferred from the factual basis; and, proper disclosure.

[443] Dr Loftsson's evidence, based on his detailed review of the Patent, is that it sets out the facts and the rationale which support a reasonable hypothesis that the formulations and compositions would be self-preserved and would pass USP preservative efficacy testing.

[444] I agree that the Patent provides a factual basis and a sound line of reasoning that self-preserved formulations would result.

[445] In addition, the '370 provides the proper disclosure; the specification clearly describes the nature of the invention and how it can be made. The specification also discloses the test results for various formulations and provides over 30 examples.

[446] As a result, I find that the allegation of lack of soundly predicted utility is not justified.

XV. CONCLUSIONS AND COSTS

[447] For the reasons set out above, I find that the allegation as to invalidity of the '370 Patent on the ground of obviousness to be justified. However, I find that the allegation of lack of demonstrated or soundly predicted utility is not justified, based on my finding that the promised utility is to provide a self preserved ophthalmic formulation without BAK that passes the USP preservative efficacy testing and provides another choice for ophthalmic formulations.

[448] With respect to costs, the respondent, Apotex, is entitled to costs to be assessed at the middle of Column IV of Tariff B.

[449] I commend the parties for their thorough submissions and organization of the extensive evidentiary record. The provision of day books and compendia is very helpful.

[450] The Judgment was issued publicly on August 11, 2014, dismissing the application for prohibition and awarding costs to the respondent.

[451] The Reasons for Judgment will be issued publicly following redactions to be proposed by the parties. Submissions on proposed redactions should be made within 15 days of the issuance of this Judgment with an additional five days for each party to respond to the submissions of the other party.

"Catherine M. Kane"
Judge

Ottawa, Ontario
Public Reasons for Judgment, August 25, 2014
Confidential Reasons for Judgment, August 11, 2014

FEDERAL COURT

SOLICITORS OF RECORD

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