IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

ALLERGAN, INC., and ALLERGAN SALES, LLC., Plaintiffs, v. ALCON INC., ALCON LABORATORIES, INC., and ALCON RESEARCH, LTD., Defendants.	**Civil Action No: 04-968-GMS**

MEMORANDUM IN SUPPORT OF ALCON'S PROPOSED CLAIMS CONSTRUCTION

Josy W. Ingersoll (No. 1088)
John W. Shaw (No. 3362)
Karen E. Keller (No. 4489)
YOUNG CONAWAY STARGATT & TAYLOR, LLP
The Brandywine Building
1000 West Street
Wilmington, Delaware 19801
(302) 571-6600
Email: kkeller@ycst.com
Attorneys for Alcon, Inc., Alcon Laboratories, Inc., and Alcon Research, Ltd.

OF COUNSEL:

Daniel J. Thomasch
Brian D. Coggio
M. Veronica Mullally
ORRICK, HERRINGTON & SUTCLIFFE LLP
666 Fifth Avenue
New York, NY 10103
(212) 506-5000

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STATUTE

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Defendants, Alcon, Inc., Alcon Laboratories, Inc., and Alcon Research, Ltd. (collectively "Alcon"), respectfully submit their opening brief on claims construction in this patent infringement action instituted by plaintiffs, Allergan, Inc. and Allergan Sales, LLC (collectively "Allergan").[1]

I. PRELIMINARY STATEMENT

This action involves Allergan's allegations that Alcon's proposed brimonidine tartrate drug product will infringe claims of Allergan's U.S. Patents Nos. 6,673,337 ("the '337 patent") and 6,641,834 ("the '834 patent").[2] The two patents-in-suit derive from the same parent application and contain the same specification, and both patents claim a "therapeutically effective" ophthalmic composition of, inter alia, brimonidine tartrate (the active ingredient of a composition intended to lower intraocular pressure). The claims of the '337 patent require that the therapeutically effective ophthalmic composition contain a so-called "solubililty enhancing component" ("SEC") present in an amount effective to increase the solubility of the active ingredient relative to its solubility in an otherwise identical composition without the SEC. The '834 patent claims a "therapeutically effective" ophthalmic composition having up to about 0.15% (w/v) of, inter alia, brimonidine tartrate, formulated at a pH of 7.0 or greater, wherein the active ingredient is soluble at 21°C.

As reflected by the Joint Claim Chart filed with the Court on April 20, 2005, there is only one claim term of the '337 patent in dispute, and there are three disputed claim terms in the '834

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[1] With the explicit permission of the Court, Alcon is concurrently submitting a motion for summary judgment that its proposed brimonidine drug product does not infringe the asserted claims of the '337 patent, and that the '834 patent is invalid for failure to satisfy the written description requirement of section 112. D.I. 30 at ¶8(a). The motion as to the '337 patent involves the interpretation of the claims of that patent, and thus, the arguments herein are directly relevant to the issues raised in that motion.

[2] The '337 and '834 patents are attached hereto as Exhibits A and B, respectively.

patent. The dispute involving the '337 patent limitation is case dispositive if decided in Alcon's favor. As shown in Alcon's accompanying memorandum in support of its motion for summary judgment, Allergan is alleging that a known viscosity agent called povidone (polyvinylpyrrolidone) acts as an SEC within the meaning of that claim term in the '337 patent. Alcon's position on the critical '337 claim construction issue is based on a series of Allergan's representations to the PTO about what is and what is not an SEC made during the prosecution of the Parent Application to the '337 patent. To distinguish prior art, Allergan specifically represented to the United States Patent and Trademark Office ("PTO") in the prosecution of the parent application that povidone (and other non-ionic viscosity agents) increased a solution's viscosity but did not have the characteristics of the claimed SECs. But now, Allergan is ignoring those representations and is attempting to recapture subject matter that it surrendered during prosecution. That is improper, as patentees cannot make representations to the PTO to secure the monopoly afforded by a patent, but then urge a materially different position in infringement litigation.

Thus, Alcon respectfully submits that the Court should construe the disputed term of the '337 patent consistent with the relevant prosecution history, as follows:

> The term "solubility enhancing component" in the '337 patent refers only to an anionic component and does not include polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers or hydroxymethylcellulose, which were expressly disclaimed during prosecution.

The '834 claims construction issues have no relevence to, or connection with, Alcon's summary judgment motion as to the invalidity of the '834 patent (based on lack of written

description).[3] While not case dispositive, the basis for Alcon's claim construction positions on '834 patent is also rooted in representations by Allergan to the PTO. During prosecution of the '834 patent, Allergan argued that it had discovered that a specific concentration of brimonidine tartrate (0.15% (w/v)) had "unexpected" properties at a particular pH (7.0 or greater) and temperature (21° C). Having so argued, and having failed to claim any range of values or measurements, Allergan cannot now materially broaden the scope of the asserted claims by relying on an undefined meaning of the term "about." Given the absence of any clear definition in the specification, Alcon contends that accepted scientific practice would be to define the values at issue in the most straightforward way possible – the range of values would be rounded to the values claimed in the patent.

Thus, in the event that the Court reaches the '834 claim construction issues, Alcon respectfully requests the following constructions:

> The term "about 0.15% (w/v)" in the '834 patent means 0.15% ± 0.005% (w/v) (likewise, "up to about 0.15% (w/v)" means up to 0.155% (w/v) (the upper limit of 0.15 ± 0.005% (w/v)).
>
> The term "pH of about 7.0 or greater" in the '834 patent means pH of 6.95 (the lower limit of 7.0 ± 0.05) or greater.
>
> The term "about 21° C" in the '834 patent means 21° C ± 0.5° C.

II. BACKGROUND

It was well known in the art that alpha-2-adrenergic agonists, including brimonidine tartrate, could be used to treat ophthalmic disorders such as elevated intraocular pressure. In fact, Allergan had marketed a product (Alphagan®) containing 0.2% brimonidine tartrate for

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[3] While the '834 patent is invalid for inadequate written description of the claimed invention of a therapeutically effective ophthalmic composition containing up to "about 0.15% (w/v)" brimonidine tartrate, the summary judgment motion does not depend on any particular definition or range of values being ascribed to the term "about 0.15% (w/v)," as the specification

years before it even applied for the patents-in-suit. But when that product was facing generic competition, Allergan began research to identify a different formulation of brimonidine tartrate in an effort to extend its brimonidine franchise and secure market exclusivity for a "newly-devised" formulation. The resulting product, Alphagan®P, differs from Alphagan® in four respects: one known viscosity agent, PVA, in Alphagan® was replaced by another, CMC, which Allergan calls a solubility enhancing component; the pH of the composition was increased from 6.5 to 7.2 and greater; a different patented preservative was used; and the amount of active ingredient was reduced from 0.2% (w/v) to 0.15% (w/v). Both patents-in-suit arose directly from these market-driven research efforts.

III. THE PERTINENT LAW

Claim construction is a question of law for the Court. Markman v. Westview Instruments, Inc., 52 F.3d 967, 979 (Fed. Cir. 1995) (en banc), aff'd, 517 U.S. 370 (1996). "Proper claim construction entails an analysis of a patent record's intrinsic evidence – the claim language, the written description, and the prosecution history." Hockerson-Halberstadt, Inc. v. Avia Group Int'l., Inc., 222 F.3d 951, 955 (Fed. Cir. 2000).

"Claim construction analysis begins with the claim language itself. As a starting point, the court gives claim terms their ordinary and accustomed meaning as understood by one of ordinary skill in the art." Id. (citations omitted). The court may consult dictionaries, encyclopedias, and treatises in determining the ordinary and customary meaning of claim terms. Genzyme Corp. v. Transkaryotic Therapies, Inc., 346 F.3d 1094, 1098 (Fed. Cir. 2003); Anchor Wall Sys., Inc. v. Rockwood Retaining Walls, Inc., 340 F.3d 1298, 1306 (Fed. Cir. 2003). Technical treatises and dictionaries, even though extrinsic evidence, are also treated as special

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and originally-filed claims are devoid of any indication that the inventors treated any specific dose or range of active ingredient to be their invention.

resources. Judges may consult such resources at any time to elucidate the underlying technology, and may also rely on dictionary definitions to construe claim terms, provided the dictionary definition does not contradict any definition established by the intrinsic evidence. Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1584 n.6 (Fed. Cir. 1996); accord, Interactive Gift Express, Inc. v. Compuserve Inc., 256 F.3d 1323, 1332 n.1 (Fed. Cir. 2001).

An examination of the specification "is necessary to determine whether the patentee has disclaimed subject matter or has otherwise limited the scope of the claims." Anchor Wall, 340 F.3d at 1306. For example, the ordinary meaning of a term is not controlling when "the patentee chooses to be his or her own lexicographer by clearly setting forth a definition for a claim term in the specification." Id. "The specification acts as a dictionary 'when it expressly defines terms used in the claims or when it defines terms by implication.'" Bell Atl. Network Serv., Inc. v. Covad Communications Group, Inc., 262 F.3d 1258, 1268 (Fed. Cir. 2001) (quoting Vitronics Corp., 90 F.3d at 1582).

The prosecution history must also be examined to determine the meaning of claim terms and whether the patentee has limited the interpretation of the terms by disclaimers made during prosecution. Rheox, Inc. v. Entact, Inc., 276 F.3d 1319, 1325 (Fed. Cir. 2002); see also Genzyme Corp., 346 F.3d at 1101 ("During prosecution, the applicant also made arguments to overcome prior art that are inconsistent with a broad interpretation of the claim term. . ."). "[S]ince, by distinguishing the claimed invention over the prior art, an applicant is indicating what the claims do not cover, he is by implication surrendering such protection." Ekchian v. Home Depot, Inc., 104 F.3d 1299, 1304 (Fed. Cir. 1997).

Sound public policy supports the Federal Circuit's rulings that explicit arguments made during prosecution can lead to narrow claim interpretation. "The public has a right to rely on

such definitive statements made during prosecution. Notice is an important function of the patent prosecution process, as reflected by the statute itself." Digital Biometrics, Inc. v. Indentix, Inc., 149 F.3d 1335, 1347 (Fed. Cir. 1998). Patentees such as Allergan "cannot during subsequent litigation escape reliance [by the defendant] upon this unambiguous surrender of subject matter." Spectrum Int'l, Inc. v. Sterilite Corp., 164 F.3d 1372, 1379 (Fed. Cir. 1998) (quoting Southwall Techs. Inc. v. Cardinal IG Co., 54 F.3d 1570, 1581 (Fed. Cir. 1995)). This maxim applies with equal force to representations made regarding the scope of an invention during the prosecution of related patent applications. Microsoft Corp. v. Multi-Tech Sys., Inc., 357 F.3d 1340, 1350 (Fed. Cir. 2004).

IV. CONSTRUCTION OF THE DISPUTED TERM IN THE '337 PATENT

A. Pertinent Facts

1. The Asserted Claims Of The '337 Patent In Dispute

There are seven asserted claims of the '337 patent. Claim 1, the only independent claim, reads:

> 1. A therapeutically effective ophthalmic composition comprising:
>
> an alpha-2-adrenergic agonist component in an amount effective to provide a therapeutic benefit to a patient to whom the composition is administered; and
>
> a solubility enhancing component other than a cyclodextrin in an amount effective to increase the solubility of the alpha-2-adrenergic agonist component in the composition relative to the solubility of an identical alpha-2-adrenergic agonist component in a similar composition without the solubility enhancing component.

All other asserted claims ultimately depend from claim 1. Dependent claims 2-4 specify that the alpha-2-adrenergic-agonist is selected from certain specified compounds. Claim 6 states that the composition's "solubility enhancing component" increases the solubility of the active ingredient

in a biological environment. And claims 9 and 10 specify that the claimed compositions contain an "effective amount of preservative."

2. The '337 Patent Specification

The '834 and '337 patents share the same specification, which describes the alleged invention as compositions containing alpha-2-adrenergic agonists as the active ingredient and other components that enhance their solubility (so-called "solubility enhancing components").[4]

The specification contends that there was a need for the claimed inventions because, although alpha-2-adrenergic agonists were effective in liquid compositions, they were difficult to solubilize. In the section identified as "Background Of The Invention," the specification states:[5]

> Some alpha-2-adrenergic agonist components with higher pKa's, for example, greater than about 7, tend to diffuse very well through lipid membranes at pH values near their pka [sic: pKa], because in such circumstances they are predominantly unionized in neutral to alkaline biological environments. However, some of these alpha-2-adrenergic agonist components become insoluble at neutral to alkaline biological pH's.

The specification contains three examples. Example 2 and Figure 1 (which is said to be based on that example) purportedly demonstrate that the anionic polymer carboxymethycellulose ("CMC") increases the solubility of brimonidine tartrate at certain elevated pHs under specific experimental conditions. The specification suggests that a variety of other compounds may also increase the solubility of alpha-2-adrenergic agonists. However, no compositions other than

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4 See, e.g., '337 patent (Ex. A), Detailed Description of the Invention ,col. 4, ll. 11-12; Summary of the Invention, col. 1, ll. 57-64; col. 2, ll. 13-16.

5 '337 patent (Ex. A), col. 1, ll. 38-45.

CMC are exemplified or shown to meet the rigid definition of "solubility enhancing component" ("SEC") set forth in claim 1 of the '337 patent.[6]

3. The Prosecution History Of The '337 Patent

The '834 and '337 patents have a common origin. Both patents claim the benefit of Provisional Application Serial No. 60/218,200, filed on July 14, 2000, and Application Serial No. 09/904,018 ("the Parent Application"), filed on July 10, 2001. The Parent Application matured into United States Patent No. 6,627,210 ("the '210 patent")[7] and its progeny applications matured into the two patents-in-suit. As the diagram below illustrates, the '337 patent issued from Application Serial No. 10/299,386 (a divisional application of the Parent Application), and the '834 patent issued from Application Serial No. 10/236,566 (a continuation application of the Parent Application).

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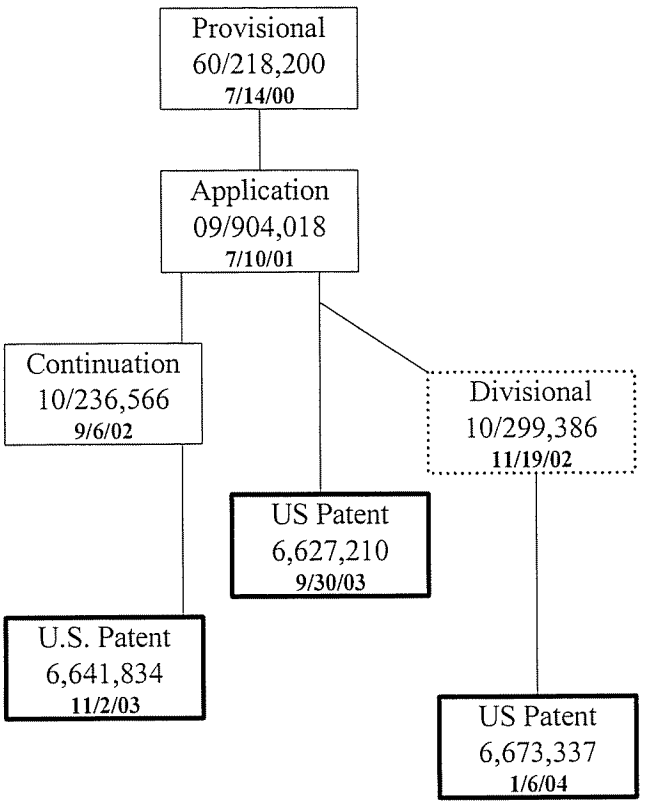
[6] Example 1 reflects the solubility of 0.5% brimonidine tartrate at various pHs to demonstrate that solubility decreases as pH increases. Example 3, five lines long, relates to Allergan's oxy-chloro preservative. '337 patent (Ex. A), col. 16, ll. 30-34.

[7] The '210 patent is attached as Exhibit C ("Ex. C").



Allergan claims a July 14, 2000 priority date for the '337 patent based on the provisional application that preceded the Parent Application. Although the '210 patent is not asserted here, its prosecution history is particularly relevant to interpreting the scope of the claims of the '337 patent. See Microsoft Corp v. Multi-Tech Sys., Inc., 357 F.3d 1340, 1350 (Fed. Cir. 2004).

a. **The Prosecution History Of The '210 Patent**

The '210 patent issued on September 30, 2003 directly from the Parent Application, which was filed on July 10, 2001.[8] In the first Office Action during its prosecution, the Examiner concluded that the original 46 claims covered four separate and distinct inventions and entered a restriction requirement that compelled the applicants to pursue prosecution of each

[8] The prosecution history ("PH") of the '210 patent is attached as Exhibit D ("Ex. D").

group in a separate patent application.[9] The applicants chose to pursue the group of claims (which matured into the '210 patent) requiring a "solubility enhancing component" (part of an aqueous liquid carrier for the active ingredient) in the Parent Application, and filed a divisional application (which matured into the '337 patent) to pursue claims requiring a preservative.[10]

Accordingly, prosecution of the Parent Application proceeded on claims 1-30 of the original application. Then pending claim 1, which is nearly identical to issued claim 1 of the '337 patent, read:[11]

> A composition comprising:
>
> an alpha-2-adrenergic agonist component in an amount effective to provide a therapeutic benefit to a patient to whom the composition is administered;
>
> a solubility enhancing component in an amount effective to increase the solubility of the alpha-2-adrenergic agonist component in the composition relative to the solubility of an identical alpha-2-adrenergic agonist component in a similar composition without the solubility enhancing component; and
>
> a liquid carrier component.

In the first substantive Office Action, the Examiner rejected all pending claims as obvious over Burke (U.S. Patent No. 5,215,991), which is assigned to Allergan, in view of Remington's Pharmaceutical Sciences.[12] The Examiner stated that it would have been obvious for an ordinarily skilled artisan to modify Burke's alpha-2-adrenergic agonist compositions by adding sodium carboxymethylcellulose ("CMC") (Allergan's purported SEC) as taught by

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9 '210 PH (Ex. D), Office Action dated September 16, 2002, Tab 4 at 1-3.

10 See '210 PH (Ex. D), Response to Restriction Requirement mailed October 16, 2002, Tab 6; '337 PH (Ex. E), Preliminary Amendment mailed November 19, 2002, Tab 2 at 1-3.

11 See '210 PH (Ex. D), Application filed July 9, 2001, Tab 1 at 33 (emphasis added).

12 '210 PH (Ex. D), Office Action dated January 9, 2003, Tab 7 at 3-5. The Burke patent and Remington's Pharmaceutical Sciences are attached as Ex. H and Ex. I, respectively.

Remington. She failed to recognize, however, that no such combination was necessary. The Burke reference itself disclosed the use of CMC in brimonidine compositions (as well as other viscosity agents) and, consequently, anticipated the pending claims.[13]

At a subsequent interview, in an apparent effort to distinguish the anticipatory disclosure of Burke, Allergan's attorney argued that the pending claims were to "an invention of selection."[14] The attorney agreed to file a declaration showing unexpected results with regard to the "anionic solubility enhancing" agent in an attempt to distinguish it from the other identified viscosity agents (all non-ionic), as a basis upon which to argue that its selection would not have been obvious to those skilled in the art.[15]

The applicants submitted a written response to the Office Action shortly thereafter.[16] In an effort to overcome the obviousness rejection, the applicants amended the claims to require that the "solubility enhancing component" be "polyanionic" or "anionic." They also acknowledged that the Burke reference disclosed brimonidine formulations with various "vehicles," including: polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers, carboxymethylcellulose (CMC), and hydroxyethylcellulose. They forcefully distinguished the claimed invention from the disclosure of Burke by arguing that anionic components (such as CMC) had unexpected properties that non-anionic vehicles (polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers, and hydroxyethylcellulose) did not:[17]

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13 See Burke patent (Ex. H), col. 5, ll. 30-34.

14 '210 PH (Ex. D), Summary of Interview dated February 25, 2003, Tab 8.

15 Id.

16 See '210 PH (Ex. D), Reply to Office Action mailed March 11, 2003, Tab 10.

17 Id. at 6 (emphasis added).

> Of the "vehicles" specifically disclosed by the Burke patent, all will function to increase the viscosity of a liquid aqueous composition. However, of these vehicles only carboxymethylcellulose (CMC) is an anionic polymer. All of the other polymers are non-ionic. They may act to increase the solution's viscosity, but they do not have the same characteristics as an anionic polymer such as CMC.

This was the basis for the applicants arguing that they had made an invention of selection.[18] In other words, the applicants stressed that it was inventive to select the anionic component disclosed in Burke (CMC) – as opposed to the other five non-ionic "vehicles" listed in Burke – to formulate a brimonidine tartrate composition.

The applicants relied on a declaration from the lead inventor, Orest Olejnik, Ph.D, in support of this argument. Like the applicants' attorney, Dr. Olejnik acknowledged that the Burke patent discloses brimonidine formulations with various "vehicles," including: polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers, carboxymethylcellulose (CMC), and hydroxyethylcellulose.[19] Yet, Olejnik represented to the PTO that Burke would not have motivated a person skilled in the art specifically to select CMC to formulate a brimonidine tartrate composition. Dr. Olejnik opined that CMC was fundamentally different from the other vehicles disclosed in Burke because it was anionic rather than non-ionic:

> Unlike the other listed polymers (polyvinyl alcohol, povidone, (polyvinylpyrollidone), hydroxypropylcellulose, poloxamers, and hydroxyethylcellulose), CMC is anionic at pH 7 or greater. The other listed polymers are non-ionic polymers. I have discovered . . . that CMC possesses the surprising advantages of both increasing

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[18] Id. at 7 ("Burke contains no disclosure that would direct or motivate the person of ordinary skill in the art to select or want to select an anionic polymeric solubility enhancing component such as CMC from the list of optional viscous 'vehicles' contained in the [Burke reference]." (emphasis added)).

[19] '210 PH (Ex. D), Declaration of Orest Olejnik, Ph.D. received March 17, 2003, Tab 11 at ¶ 4.

> the solubility of brimonidine in solution . . . and causing such solutions to have superior adherence to cell surfaces, including ocular surfaces such as the cornea.[20]

Furthermore, Dr. Olejnik stated that the non-ionic vehicles disclosed in Burke would not work in his invention:

> It is also my belief that brimonidine solutions made using the other "vehicles" mentioned in the Burke patent would not possess this surprising combination of advantages. Therefore, the disclosures of Burke and Remington's in no way would render the presently claimed compositions obvious to the worker of ordinary (or even extraordinary) skill in the art.[21]

The Examiner allowed the claims to issue without further prosecution.

b. The Prosecution History Of The '337 Patent

The '337 patent issued on January 6, 2004 from a divisional application filed on November 19, 2002 of the Parent Application.[22] As mentioned above, the divisional application was purportedly filed to pursue claims from the Parent Application involving compositions containing an oxy-chloro preservative.

In the first Office Action, the Examiner rejected the pending claims as obvious over the Burke patent in view of Beck et al. (U.S. Patent No. 6,358,935).[23] She observed that it would have been obvious to modify the compositions disclosed in Burke by substituting the chlorite preservative disclosed in Beck.[24]

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20 Id. at ¶ 7 (emphasis added).

21 Id. at ¶ 8 (emphasis added).

22 The prosecution history ("PH") of the '337 patent is attached as Exhibit E ("Ex. E").

23 The Beck et al. patent is attached as Exhibit G ("Ex. G"). It should be noted that Edward Kerslake, co-inventor on the patents-in-suit, is also an inventor on the Beck patent.

24 '337 PH (Ex. E), Office Action dated March 3, 2003, Tab 3 at 3-5.

In response, Allergan broadened the claims by eliminating from all claims the requirement for an oxy-chloro preservative, despite the fact this was the very reason the divisional application was filed.[25] Allergan also amended the claims by adding the SEC limitation.[26] As amended, the pending claims of the divisional application were effectively the same as the claims the Examiner had rejected in the Parent Application over the Burke disclosure (which were allowed only after they were limited to compositions containing "anionic" SECs).

Consistent with their response in the Parent Application, the applicants acknowledged that "Burke discloses that the combinations claimed may optionally be formulated using various vehicles, including carboxymethyl cellulose [CMC], various tonicity agents, and various preservatives, including benzalkonium chloride."[27] The applicants, however, ignored their prior representations that the non-anionic "vehicles" disclosed in Burke would not function in their invention. To the contrary, they argued:[28]

> Applicants respectfully maintain that for all its discussion of possible formulations, nothing in Burke discloses or suggests the use of a solubility enhancing component in combination with an alpha adrenergic agonist. The present application, which also discloses the advantages of using such a component (such as greater flexibility with the concentration and pH at which such composition is formulated, is, to the Applicants' knowledge, the first reference to do so.

Inexplicably, the Examiner did not identify the glaring inconsistency in Allergan's representations. The claims, which are essentially the same as those rejected during prosecution of the '210 patent over Burke, were allowed without further prosecution.

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25 '337 PH (Ex. E), Reply to Office Action mailed June 13, 2003, Tab 5 at 2-3.

26 Id.

27 Id. at 5.

28 Id. (emphasis added).

B. Alcon's Construction Of The Term "Solubility Enhancing Component"

The parties' dispute with respect to the '337 patent focuses upon the scope of claim 1. Consistent with the prosecution history, Alcon contends that claim 1, and all of its dependant claims, require that the "solubility enhancing component" be "anionic." Allergan unambiguously disavowed all non-anionic compounds – and, specifically, povidone – from the scope of their invention. This disavowal during prosecution of the Parent Application that matured into the '210 patent limits the claims of the '337 patent to the same scope. See Microsoft, 357 F.3d at 1350 ("Any statement of the patentee in the prosecution of a related application as to the scope of the invention [is] relevant to claim construction, and the relevance of the statement . . . is enhanced by the fact that it was made in an official proceeding in which the patentee has every incentive to exercise care in characterizing the scope of its invention.").

1. Allergan's Arguments Before The PTO

Immediately after representing to the Examiner that the non-ionic "vehicles" disclosed in the Burke patent would not function as SECs in its "invention of selection" (and thereby securing allowance of narrow claims limited to anionic SECs in the '210 patent), Allergan took the position in the co-pending divisional application that the Burke patent did not disclose any SECs (and thereby secured allowance of broad claims covering any SEC in the '337 patent).

Allergan's attorney reconfigured the claims and argued for the patentability of these entirely new claims after the Examiner rejected them as obvious over Burke and Beck in the initial Office Action. Allergan broadened the claims by eliminating their requirement for an oxy-chloro preservative.[29] This, eliminated the reason the Examiner had required the filing of the divisional application in the first place. Allergan also amended the claims to add the SEC limitation.

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[29] '337 PH (Ex. E), Reply to Office Action dated June 6, 2003, Tab 5 at 2-3.

Despite its prior representations during prosecution of the Parent Application, Allergan now argued that nothing in its own Burke patent disclosed the use of an SEC with an alpha adrenergic agonist.[30] That patent, however, identifies alpha-2-adrenergic agonist compositions containing at least one vehicle identified as an SEC in the specification of the '337 patent.[31] Allergan admitted as much during the prosecution of the Parent Application just three months earlier when it acknowledged that Burke disclosed anionic CMC and actually claimed it as an SEC with "unexpected properties" relative to the other, non-ionic, "vehicles" disclosed in the Burke patent.[32] Thus, even though the Burke reference was before the Examiner, Allergan misled the Examiner as to its proper contents and did not inform the Examiner that this particular Alcon application was not the first to address, and indeed, claim brimonidine tartrate compositions containing SECs.

Thereafter, the claims of the '337 patent issued without further rejection even though they are essentially the same as the originally-filed claims of the Parent Application, which were not allowed until they were limited to anionic SECs. This is made immediately apparent when the claims are laid side-by-side, as in the table below:

Claim 1 of the '337 patent[33]	**Claim 1 of the Parent Application**[34]
1. A therapeutically effective ophthalmic composition comprising: an alpha-2-adrenergic agonist component in an	1. A composition comprising: an alpha-2-adrenergic agonist component in an

30 '337 PH (Ex. E), Response to Office Action dated June 13, 2003, Tab 5 at 5 (emphasis added).

31 See Burke Patent (Ex. H), col. 5, ll. 28-34.

32 See '210 PH (Ex. D), Reply to Office Action mailed March 12, 2003, Tab 10 at 6-7; '210 PH (Ex. D), Declaration of Orest Ojenik, Ph.D. received March 17, 2003, Tab 11.

33 '337 Patent (Ex. A), col. 16, ll. 41-52 (emphasis added).

34 '210 PH (Ex. D), Application filed July 10, 2001, Tab 1 at 33 (emphasis added).

amount effective to provide a therapeutic benefit to a patient to whom the composition is administered; a solubility enhancing component other than a cyclodextrin in an amount effective to increase the solubility of the alpha-2-adrenergic agonist component in the composition relative to the solubility of an identical alpha-2-adrenergic agonist component in a similar composition without the solubility enhancing component.	amount effective to provide a therapeutic benefit to a patient to whom the composition is administered; a solubility enhancing component in an amount effective to increase the solubility of the alpha-2-adrenergic agonist component in the composition relative to the solubility of an identical alpha-2-adrenergic agonist component in a similar composition without the solubility enhancing component; and a liquid carrier component.

2. The Claims Of The '337 Patent Are Limited By Allergan's Representations

In construing the claims, the "[c]laim language . . . must be read consistently with the totality of the patent's applicable prosecution history." Biovail Corp. Int'l v. Andrx Pharm., Inc., 239 F.3d 1297, 1301 (Fed. Cir. 2001). Because the '337 patent and the '210 patent share a common specification and derive from the same Parent Application, the prosecution history of the Parent Application leading to the '210 parent patent is equally relevant in construing the claims of the '337 patent. See Jonsson v. Stanley Works, 903 F.2d 812, 818 (Fed. Cir. 1990). Thus, representations during the '210 patent's prosecution by Allergan and one of its inventors (Dr. Olejnik) limit the scope of the invention to compositions containing anionic SECs. These representations were made to overcome the prior art Burke patent and are equally relevant to interpreting the claims in the '337 patent. Id. ("[T]he prosecution history (or file wrapper) limits the interpretation of claims so as to exclude any interpretation that may have been disclaimed or disavowed during prosecution in order to obtain claim allowance."); see also, Microsoft Corp., 357 F.3d at 1347 ("A patentee may also limit the scope of the claims by disclaiming a particular interpretation during prosecution."); ACCO Brands Inc. v. Micro Security Devices Inc., 346 F.3d 1075, 1078 (Fed. Cir. 2003) ("Statements made during prosecution which clearly disclaim a

particular claim interpretation will limit the scope of the claims."); Omega Eng'g, Inc. v. Raytek Corp., 334 F.3d 1314, 1324 (Fed. Cir. 2003) ("[W]here the patentee has unequivocally disavowed a certain meaning to obtain his patent, the doctrine of prosecution disclaimer attaches and narrows the ordinary meaning of the claim congruent with the scope of the surrender.").

Because Allergan unambiguously characterized the invention as limited to compositions with anionic SECs and explicitly disclaimed all non-anionic SECs (including povidone), the term SEC in the '337 patent should also be limited to anionic SECs. See Elkay Mfg. Co. v. Ebco Mfg. Co., 192 F.3d 973, 980 (Fed. Cir. 1999) ("When multiple patents derive from the same initial application, the prosecution history regarding a claim limitation in any patent that has issued applies with equal force to subsequently issued patents that contain the same claim limitation.").

Furthermore, the term SEC appears in precisely the same context in the '337 patent as it does in the '210 patent. Thus, any prosecution history relating to that term in the '210 patent applies with equal force to that limitation in the '337 patent. See Wang Labs., Inc. v. Am. Online, Inc., 197 F.3d 1377, 1384 (Fed. Cir. 1999) (characterization of the invention in prosecution history of a parent application applies to common subject matter in continuation-in-part application); Biovail, 239 F.3d at 1302 (prosecution history relating to a claim limitation applies with equal force to the same limitation appearing in a similar context in a related patent). For example, noting that the claim limitation "admixture" appeared in a similar context in both the '505 and the '791 patents, the Biovail court held that "any prosecution history relating to the 'admixture' limitation of the '505 patent . . . [applied] with equal force to that limitation in . . . the '791 patent." Id. Even though neither the claims nor the specification of either patent required that the admixture be homogeneous, the court held that statements in the prosecution

history describing the "admixture" as homogeneous in the '505 patent required that the term "admixture" in '791 patent be similarly construed and limited to a homogeneous admixture. Similarly, in this case, the term SEC should be limited to anionic SECs (as it was in the '210 patent) because of Allergan's explicit statements in the earlier prosecution regarding the same claim limitation. Indeed, Alcon not only limited the claims to anionic SECs, it explicitly distinguished, and in doing so disclaimed, povidone.

Allergan also cannot claim non-ionic SECs (e.g., povidone) because it expressly stated that such compounds were not part of its "invention." In Microsoft, for example, the Federal Circuit limited the scope of the claims in three patents-in-suit based on the patentee's characterization of its invention in response to an obviousness rejection in the prosecution history (among other things). Microsoft Corp., 357 F.3d at 1349. As here, the patents-in-suit were derived from the same parent application and shared a common specification. The Federal Circuit held that it could not "construe the claims to cover subject matter broader than that which the patentee itself regarded as comprising its inventions and represented to the PTO" and that "[a]ny statement of the patentee in the prosecution of a related application as to the scope of the invention would be relevant to claim construction. . . ." Id. at 1349-50. Likewise, the prosecution history of the '210 parent patent is replete with statements by Allergan and one of the inventors disclaiming all SECs other than anionic SECs. Moreover, the prosecution explains how only anionic polymers will function as SECs and refers to portions of the common specification to support the anionic nature of the SECs in the invention. Thus, the claim term "SEC" in the '337 patent should be interpreted as limited to anionic SECs consistent with how Allergan and at least one of the named inventors reviewed the scope of the "invention."

The fact that the term "SEC" is expressly limited to an "anionic SEC" in the '210 patent does not prevent a similar interpretation of the term in the '337 patent because the prosecution histories of both patents so clearly demonstrate that the scope of the invention claimed in the '337 patent should also be limited to anionic SECs. See Modine Mfg. Co. v. United States Int'l Trade Comm'n, 75 F.3d 1545, 1551 (Fed. Cir. 1996) (["I]t is incorrect to construe a claim as encompassing the scope that was relinquished in order to obtain allowance of another claim, despite a difference in the words used."); Microsoft Corp., 357 F.3d at 1349 (The court "cannot construe the claims to cover subject matter broader than that which the patentee itself regarded as comprising its inventions and represented to the PTO."). Not only did Allergan limit the term SEC to anionic SECs, but it expressly disclaimed certain enumerated SECs. It cannot now avoid the effect of such disclaimers. See Omega Eng'g Inc., 334 F.3d at 1324 ("As a basic principle of claim interpretation, prosecution disclaimer promotes the public notice function of the intrinsic evidence and protects the public's reliance on definitive statements made during prosecution."); Spectrum Int'l, 164 F.3d at 1378-79 (defendant had "a right to rely on such definitive statements made during prosecution" concerning "what the claims do not cover").

Because the claims of the '337 patent cannot cover more than the alleged invention that Allergan itself regarded as its discovery, the term "SEC" should be construed to include only anionic SECs. Moreover, Allergan should not be allowed now to recapture the non-ionic "vehicles" (e.g., polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers or hydroxymethylcellulose) that it affirmatively disavowed during prosecution.

V. CONSTRUCTION OF THE DISPUTED TERMS IN THE '834 PATENT

A. Pertinent Facts

1. The Asserted Claims Of The '834 Patent

There are 16 asserted claims of the '834 patent. Claim 1, which is one of the patent's two independent claims, reads:

> 1. A therapeutically effective aqueous ophthalmic composition comprising:
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> up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate, the composition having a pH of about 7.0 or greater, and the 5-bromo-6-(2-imidozolin-2-yalmino) quinoxaline tartrate being soluble in the composition at about 21°C.

Claims 2-6, 8, and 9 depend from claim 1. Claims 2, 3, and 4 specify that the claimed compositions include "up to 0.15%," "about 0.15%," or "0.15%" of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate, respectively. All require that the pH is "about 7.0 or greater" and the active ingredient is soluble at 21° C. Claim 5 specifies a "pH of 7.0 or greater." And claims 6, 8, and 9 specify that the claimed compositions contain a particular preservative, are substantially free of cellulosic derivatives, or substantially free of carboxymethyl cellulose, respectively.

Claim 10, the patent's other independent claim, reads:

> 10. A therapeutically effective aqueous ophthalmic composition comprising:
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> up to about 0.15% (w/v) of a component selected from the group consisting of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, salts of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, esters of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, and mixtures thereof, the composition having a pH of about 7.0 or greater, and the component being soluble in the composition at about 21°C.

The remaining claims (claims 11-14, 17, 18, and 20), which are dependent on claim 10, specify the same parameters as the corresponding claims depending from claim 1, discussed above.

2. The '834 Patent Specification

The specification of the '834 patent, as previously noted, is identical to that of the '337 patent. As relevant here, the specification provides no guidance as to the meaning of the term "about" as used on the three disputed terms. Indeed, it never mentions the 0.15% (w/v) concentration.

3. The Prosecution History Of The '834 Patent

The '834 patent issued on November 4, 2003 from a continuation application of the Parent Application filed on September 6, 2002.[35] A preliminary amendment accompanied that filing and cancelled all claims originally contained in the Parent Application. The preliminary amendment also introduced 19 new claims drawn to compositions of "up to about 0.15%(w/v) [brimonidine] tartrate" at about pH 7.0 and soluble at 21° C.[36] This "0.15%" value did not appear in any of the earlier applications or prosecution.

In the first Office Action, the Examiner rejected the claims as obvious over the Burke patent. He recognized that Burke disclosed the claims' elements (except the chloride component) and that an ordinarily skilled artisan could determine the most efficacious dose by carrying out a dose response curve.[37] As to certain dependent claims, the Examiner observed that it would have been obvious for one skilled in the art to modify the compositions of Burke by substituting the preservative disclosed in the Beck patent.[38]

Allergan's counsel and the Examiner had a telephonic interview shortly thereafter. There, Allergan stressed, for the first time, the allegedly unexpected advantages of a composition

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35 The prosecution history ("PH") of the '834 patent is attached as Exhibit F ("Ex. F").

36 '834 PH (Ex. F), Preliminary Amendment filed September 6, 2002, Tab 2.

37 '834 PH (Ex. F), Office Action dated December 10, 2002, Tab 4 at 4-5.

38 Id. at 5.

comprising up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinozaline tartrate with a pH of about 7.0 or greater.[39] Faced with the Examiner's apparent skepticism, Allergan agreed to file a declaration demonstrating the "unexpected results" of the newly-claimed compositions.[40]

In its written reply to the Office Action, Allergan noted that prior art "brimonidine solutions for ophthalmic use have been formulated at a pH of about 6.3-6.5 and a concentration of 0.2% (w/v)."[41] Then, in an effort to distinguish the prior art compositions, Allergan argued that:

> The present invention is the result of the surprising finding that increasing the pH of a brimonidine solution to a pH of greater than about 7.0 leads to similar efficacy at a 25% lower concentration (from 0.2% (w/v) to about 0.15% (w/v) or less) than is seen in a brimonidine solution at a pH of about 6.6-6.8. This appears to be due to the fact that at a pH closer to the pKa of brimonidine (which has a pKa of about 7.4) than pH 6.3-6.5, a larger proportion of the molecules are electrostatically neutral, and thus less lipophobic than the polarized molecule.[42]

Allergan built upon this "surprising finding" by arguing:

> However, it is particularly surprising that such a therapeutically effective dosage of brimonidine could be formulated in aqueous solution at a pH greater than about 7.0. Figure 1 of the present specification shows that brimonidine's solubility decreases precipitously at pH values above 7.0. The fact that a therapeutically effective dosage could be provided by a composition containing about 0.15% or less of brimonidine at such pH values is truly unexpected.[43]

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39 '834 PH (Ex. F), Summary of Interview dated February 25, 2003, Tab 5.

40 Id.

41 '834 PH (Ex. F), Reply to Office Action mailed March 17, 2003, Tab 6 at 4.

42 Id.

43 Id.

Thus, the key to the alleged invention of the '834 patent was the similar efficacy of a "25% lower concentration" of active ingredient (comparing 0.2% (w/v) to 0.15% (w/v)) when the composition was at an elevated pH (i.e., a pH of 7.0 or greater). Yet, this disclosure cannot be found anywhere in the specification or in the original claims.

Allergan also directed the Examiner's attention to a declaration from Allergan employee Amy Batoosingh that discussed an article by Katz et al.[44] According to Allergan's attorneys, the Katz article demonstrated that there was no statistically significant difference between the prior art 0.2% brimonidine formulation at pH 6.3-6.5 and a 0.15% brimonidine solution at pH 7.2 in lowering intraocular pressure.[45] Allergan argued that the use of a lower concentration of active ingredient would be advantageous because that formulation would have a reduced likelihood of side-effects, and those side-effects (if any) would be less severe.[46] It then reiterated that "the present invention is drawn to surprising new therapeutic compositions comprising at least a 25% lower concentration of brimonidine than previous ophthalmic formulations, at pH closer both to the solubility limits of bromonidine, and to the pKa of the compound."[47] But, in actuality, the 0.15% (w/v) limitation had nothing to do with the so-called invention disclosed in the specification. It was an after-the-fact attempt to cover Allergan's reformulated commercial product (Alphagan® P) and stymie generic competition. Thus, nothing in the specification or prosecution history is enlightening as to the term "about 0.15%."

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44 Id. The Declaration of Amy Batoosingh and the Katz et al. article can be found in the prosecution history of the '834 patent. See '834 PH (Ex. F), Declaration of Amy Batoosingh mailed March 17, 2003 (and accompanying Katz et al. article), Tab 7.

45 '834 PH (Ex. F), Reply to Office Action mailed March 17, 2003, Tab 6 at 4.

46 Id. at 5.

47 Id.

After requiring a further limitation of "about 21° C" to be added, the Examiner allowed the claims.

B. Alcon's Construction Of Terms In The '834 Patent

Allergan is trying to broaden the subject matter of its '834 patent in a manner unsupported by the intrinsic evidence. During prosecution of that patent, Allergan argued that it had discovered that a particular concentration of brimonidine tartrate was therapeutically effective at a particular pH and temperature.[48] But now, Allergan suggests that these values actually encompass an undefined range of values because these parameters are modified by the word "about." Allergan proposes that the word "about" should be interpreted to mean its synonym "approximately," relying on the inapposite decision in Merck & Co. v. Teva Pharm., 395 F.3d 1364 (Fed. Cir. 2004). Here, unlike in Merck, neither party proposes that "about" is defined in the specification to mean the antonym of "about" – "exactly." Nor does Alcon propose an interpretation that is inconsistent with the claim language or the other intrinsic evidence. Alcon's proposed interpretation seeks to define the range encompassed by the word "about" in tangible terms consistent with the context of the alleged "invention."

The Federal Circuit has repeatedly held that the meaning of the word "about" in a patent depends on the technological facts of the particular case and must be interpreted in its "technologic and stylistic context." Pall Corp. v. Micron Separations, Inc., 66 F.3d 1211, 1217 (Fed. Cir. 1995). Nevertheless, it is also recognized that the term "about" has a rather narrow meaning. "About" connotes "some approach to exactness in quantity, number, or time: approximately." Conopco, Inc. v. May Dep't Stores Co., 46 F.3d 1556, 1561 n.2 (Fed. Cir. 1994) (citing Webster's Third New International Dictionary). Context, of course, is critical.

In the context of the claims of the '834 patent, the terms – "about 0.15%," "pH of about 7.0," or "about 21° C" – direct the reader to the precision allowed by the context of the recited values. The concentration of brimonidine tartrate ("about 0.15%") is expressed to the hundredths of a unit, pH ("pH of about 7.0") is expressed to the tenths of a unit, and temperature ("about 21°C") is expressed in single integers. The patent's disclosure purports to use even more refined units. It reports concentrations to the tens-of-thousandths of a unit and pH to the hundredths.[49] And they indicate that small changes in concentration, pH, or temperature can have dramatic effects. To suggest that a different, more general, metric should be used to interpret the claims would ignore these crucial aides to claim interpretation.[50]

The Federal Circuit has approved of the use of experimental error (i.e., an estimation of the precision with which an experimental value can be determined) to interpret the range of values encompassed by the term "about." See B.J. Services Co. v. Halliburton Energy Serv., 338 F.3d 1368, 1372-73 (Fed. Cir. 2003) (approving patentee's interpretation of "about" as encompassing the range of experimental error in response to an indefiniteness attack); Hybritech Inc. v. Abbott Labs, 849 F.2d 1446, 1455 (Fed. Cir. 1988) (finding no error in district court's construction of the scope of "at least about 10^8 liters/mole" claim limitation based on the amount of error inherent in such measurements). Similarly, when, as here, a specification failed to provide any express guidance as to the breath of the term "about" and only disclosed a value that rounded-up to the value specified in the claim, this Court held that a limitation to "no more than

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[48] While addressed in the prosecution history of the later-filed claims, Allergan did not define in the original disclosure any concentration of the active ingredient to be "therapeutically effective."

[49] See, e.g., '834 Patent (Ex. B), Table 4, col. 15, ll. 40-65.

about 0.6 square inches" did not cover an embodiment that, rounded-off to a single digit, exceeded 0.6. See Proctor & Gamble Co. v. Paragon Trade Brands, Inc., 989 F.Supp. 547, 623-24 (D. Del. 1997); see also, Viskase Corp. v. Am. Nat'l Can Co., 261 F.3d 1316, 1320-22 (Fed. Cir. 2001) (agreeing that it is a standard scientific convention to express a rounding range when a number has not been carried to the next mathematically significant figure, but construing the claim more narrowly because of other representations made during prosecution); Minnesota Mining & Mfg. v. Beautone Specialties Co., Ltd., 117 F.Supp.2d 72, 88 (D. Mass. 1999) (interpreting the term "about" to refer to tenths when the claim reports values in those units).

Accordingly, although the '834 patent's specification and prosecution history do not explicitly define the scope of the meaning of "about," they inform its meaning. Each individual term-in-dispute is discussed in greater detail below.

1. The Term "About 0.15% (w/v)"

The narrow scope of values encompassed by the "about 0.15%" limitation is made particularly clear when one carefully examines that limitation. That is, the plain meaning of "about 0.15%" to a person skilled in the art would be 0.15% ± 0.005%. This interpretation is consistent with the other claims of the '834 patent, its specification, and that patent's prosecution history.

The specification of the '834 patent provides no teaching or suggestion as to the criticality of the 0.15% value. Indeed, that numerical value cannot be found anywhere in the patent. The specification only reflects the testing of brimonidine tartrate solutions at concentrations of 0.5% (w/v) and 0.2% (w/v). Moreover, the applications upon which the '834 patent relies do not allude to the 0.15% value either. The 0.15% value did not appear until a

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[50] This assumes, of course, that some numbers can be assigned. If "about" is so amorphous that no range of values can be ascertained (as Allergan seems to suggest), the claims should be

Preliminary Amendment was filed. Those circumstances can lead to only one conclusion: "about 0.15%" can be afforded only a very minimal range.

The 0.15% concentration was at the core of Allergan's argument for the patentability of the claims of the '834 patent. After the Examiner rejected the claims as obvious, Allergan attempted to assure her that there was something unexpectedly advantageous about using a specified concentration of brimondine tartrate.[51] Then Allergan repeated this argument – focusing again on the "special" concentration – in its written response that followed.[52] Allergan argued that it could obtain the same therapeutic effect as the well-accepted formulation of 0.2% brimonidine by using a 0.15% formulation at a higher pH. According to Allergan: "[t]he fact that a therapeutically effective dosage could be provided by a composition containing about 0.15% or less of brimonidine at such pH values is truly unexpected."[53] It reasoned that the use of such a lower concentration formulation would be advantageous because it would reduce the likelihood and/or severity of side-effects.[54] Allergan reiterated that "the present invention is drawn to surprising new therapeutic compositions comprising at least a 25% lower concentration of brimonidine than previous ophthalmic formulations, at pH closer both to the solubility limits of bromonidine, and to the pKa of the compound."[55]

Moreover, the corroborative declaration that the Examiner required to demonstrate the patentability of the claims also compared the 0.2% and 0.15% concentrations of brimonidine

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held invalid for indefiniteness.

51 '834 PH (Ex. F), Summary of Interview dated February 25, 2003, Tab 5.

52 '834 PH (Ex. F), Reply to Office Action mailed dated March 17, 2003, Tab 6 at 3-5.

53 Id.

54 Id. at 5.

55 Id. (emphasis added).

tartrate.[56] The declaration reported that "brimonidine 0.2% and brimonidine-Purite 0.15% showed comparable efficacy when each was used for the treatment of ocular hypertension in glaucoma and/or ocular hypertensive human patients over a 12 month period of time, despite a significant reduction in the concentration of the active ingredient in the latter formulation."[57] Thus, assuming the assertions made in Allergan's response to the Office Action and Ms. Batoosingh's Declaration were valid, the 0.15% brimonidine-Purite formulation was the only formulation demonstrated to satisfy the '834 patent's limitations. By Allergan's own admission, higher concentrations such as 0.2% were in the prior art and would have caused more side-effects. And lower concentrations were not shown by the applicants to be "therapeutically effective," as the claims require.

In view of the foregoing, Alcon proposes that the term "about 0.15%" be interpreted to encompass the range of values that would be rounded up or down to 0.15% (i.e., 0.15% ± 0.005%).

2. The Term "pH Of About 7.0 Or Greater"

Although the intrinsic evidence does not define "pH of about 7.0 or greater," the plain meaning of the term "about," which is consistent with its use in the specification and the prosecution history, support an interpretation of the claim term "pH of about 7.0 or greater" to mean a pH of 6.95 (the lower limit of 7.0 ± 0.05) or greater.

The plain meaning of "pH of about 7.0 or greater" would be immediately clear to a person of ordinary skill in the art (by whom the meaning of claim terms is determined). That person would know that pH is a measure of the acidity of a solution, solutions with pH values less than 7.0 are "acidic," those with pH values greater than 7.0 are "alkaline" (or "basic"), and

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56 See '834 PH (Ex. F), Declaration of Amy Batoosingh received March 24, 2003, Tab 7.

57 Id. at ¶ 4.

solutions with a pH of 7.0 are neutral (i.e., neither acidic nr alkaline).[58] An ordinarily skilled artisan would also understand that, because of the way pH is calculated, differences in single whole numbers of values (e.g., between pH 7.0 and pH 6.0) actually reflect differences of an entire order or magnitude.[59] Accordingly, a person of ordinary skill would understand "pH of about 7.0 or greater" to encompass neutral or alkaline pH values (i.e., pH values 7.0 –14.0).

The specification of the '834 patent supports Alcon's construction. For example, the specification suggests the alleged invention solved a problem. Although some alpha-2-adrenergic agonists with pKas greater than 7 (like brimonidine tartrate[60]) diffuse well through biological membranes (such as the membranes in the eye) when formulated at neutral or alkaline pHs, they are also insoluble at these pHs.[61] The alleged invention was said to enhance the efficacy of such agonists by increasing their solubility at pHs higher than neutral (i.e., greater than 7.0).[62] There is no indication that the claimed compositions should have an acidic pH (i.e., a pH less than 7.0).

The normal scientific interpretation is confirmed by reference to the prosecution history. The originally filed application had two claims specifying pH. One referred to "a pH of about 7 or greater" and the other to "a pH of about 7 to about 9."[63] Both of these claims were dependent

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58 See David W. Oxtoby & Norman N. Nachitrieb, Principles of Modern Chemistry 213 (1996) (Ex. J).

59 See e.g., B. Alberts, et. al., Molecular Biology of the Cell, G-18 (3d ed. 1994) (defining pH as a "Common measure of the acidity of a solution: 'p' refers to power of 10, 'H' to hydrogen. Defined as a the negative logarithm of the hydrogen ion concentration in moles per liter (M). Thus pH 3 (10^{-3} M H^+) is acidic and pH 9 (10^{-9} M H^+) is alkaline.)" (Ex. K).

60 "Brimonidine tartrate has a pKa of about 7.78." '834 patent (Ex. B), col. 13, ll. 16.

61 See '834 patent (Ex. B), Background of the Invention, col. 1, ll. 38-45.

62 See id., Summary of the Invention, col. 2, ll. 9-20.

63 See '834 PH (Ex. F), Application as filed September 6, 2002, Tab 1 at 36 (claims 21 and 22, respectively).

upon then pending claim 1, which covered a composition containing an alpha-2-adrenergic agonist component and a "solubility enhancing component." But the applicants requested examination of a more precise pH. Coincident with the filing of the original application, the applicants requested examination of claims limited to a particular concentration range of a particular alpha-2-adrenergic agonist component ("up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate" (claim 47) and "up to about 0.15% (w/v) of a component selected from the group consisting of [brimonidine, its salts, esters, or mixtures]" (claim 57)) having the more precise pH of "about 7.0 or greater."[64] Thus, the applicants narrowed their claim from the range that could be arguably attributed to the recitation of a whole number in the claims ("a pH of about **7** or greater") to the much narrower recitation of pH terms of tenths of that number ("a pH of about **7.0** or greater") (emphasis added).[65]

Moreover, Allergan expressly surrendered brimonidine compositions with pHs less than 7.0 during prosecution of the '834 patent. First, it surrendered compositions with pHs less than "about" 6.8 by distinguishing its high pH ("greater than about 7.0") composition from the lower pH ("about 6.6-6.8") prior art compositions:[66]

> The present invention is the result of the surprising finding that increasing the pH of a brimonidine solution to a pH of greater than about 7.0 leads to similar efficacy at a 25% lower concentration (from 0.2%(w/v) to about 0.15%(w/v) or less) than is seen in a brimonidine solution at a pH of about 6.6-6.8.

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64 '834 PH (Ex. F), Preliminary Amendment dated September 6, 2002, Tab 2 at 1-3.

65 Indeed, the remainder of the prosecution of the '834 patent was focused on the numbers varying around tenths of the whole number. For example, in summarizing an interview with the applicants, the Examiner noted that the applicants would file a declaration to demonstrate the purportedly unexpected advantages of such a composition having "a pH of 7.0 or greater." '834 PH (Ex. F), Summary of Interview dated February 25, 2003, Tab 5.

66 '834 PH (Ex. F), Reply to Office Action mailed March 17, 2003, Tab 6 at 4.

Then, drawing upon the specification and accompanying declaration of Amy Batoosingh for support, it repeatedly emphasized that its claims were directed to compositions with pH values greater than 7.0. Allergan stated that Figure 1 of the specification "shows that brimonidine's solubility decreases precipitously at pH values above 7.0" and argued that "[t]he fact that a therapeutically effective dosage could be provided by a composition containing about 0.15% or less brimonidine at such pH values is truly unexpected." Id. (emphasis added). Likewise, Ms. Batoosingh's declaration stated that the 0.15% brimonidine-Purite composition in the Katz article had a pH greater than 7.0 (i.e., "pH 7.1-7.3").[67]

Accordingly, Alcon proposes that the term "pH of about 7.0" be interpreted to the encompass the full range of values that would be rounded up or down to that number (i.e., 7.0± 0.05). Any broader interpretation of "pH of about 7.0" would be contrary to scientific principles, binding precedent, and a fair reading of the relevant evidence.

3. The Term "About 21° C"

The specification (including the claims as originally filed) and the prosecution history of the '834 patent provide no express teaching regarding the scope of the temperature limitation. Thus, Alcon proposes that the term "about" be interpreted to encompass the full range of values that would normally be rounded up or down to a temperature of 21° C (i.e., 21°C ± 0.5° C).

This interpretation is consistent with well-recognized scientific principles. It is important to note that a variation of 0.5° C spans a rather large, easily measurable, temperature range. In fact, one-half-of-one degree (i.e., 0.5) in the Celsius scale is nearly equivalent to an entire degree

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[67] '834 PH (Ex. F), Declaration of Amy Batoosingh received March 24, 2003, Tab 7 at ¶ 3. (emphasis added).

in the more familiar Fahrenheit scale.[68] Accordingly, Alcon's proposed interpretation of "about 21° C" as 21°C ± 0.5° C provides a generous scope to the claim.

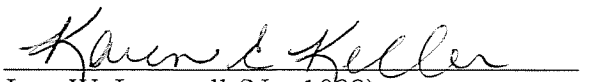
VI. CONCLUSION

For the foregoing reasons, the Court should construe the disputed claim terms in accordance with Alcon's proposed constructions.

Dated: May 2, 2005

Respectfully submitted,

Young Conaway Stargatt & Taylor, LLP



Josy W. Ingersoll (No. 1088)
John W. Shaw (No. 3362)
Karen E. Keller (No. 4489)
The Brandywine Building
1000 West Street
Wilmington, Delaware 19801
(302) 571-6600
Email: kkeller@ycst.com

Attorneys for defendants
Alcon, Inc., Alcon Laboratories Inc.,
and Alcon Research, Ltd.

Of Counsel

Daniel J. Thomasch
Brian D. Coggio
M. Veronica Mullally
Orrick, Herrington & Sutcliffe LLP
666 Fifth Avenue
New York, NY 10103
(212) 506-5000

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[68] The formula for converting to Fahrenheit from Celsius is $^{o}F = 9/5\ (^{o}C) + 32$. See Webster's Deluxe Unabridged Dictionary 291 (1983) (Ex. L).

CERTIFICATE OF SERVICE

I, Karen E. Keller, Esquire hereby certify that on May 2, 2005, I caused to be electronically filed a true and correct copy of the foregoing document with the Clerk of the Court using CM/ECF, which will send notification that such filing is available for viewing and downloading to the following counsel of record:

William J. Marsden, Jr., Esquire
Fish & Richardson, P.A.
919 N. Market Street, Suite 1100
Wilmington, DE 19801

I further certify that on May 2, 2005, I caused a copy of the foregoing document to be served by hand delivery on the above-listed counsel of record and on the following non-registered participants in the manner indicated:

BY FEDERAL EXPRESS

Jonathan E. Singer, Esquire
Fish & Richardson, P.A.
3300 Dain Rauscher Plaza
60 South Sixth Street
Minneapolis, MN 55402

YOUNG CONAWAY STARGATT & TAYLOR, LLP

Karen E. Keller

Josy W. Ingersoll (No. 1088)
Karen E. Keller (No. 4489)
The Brandywine Building
1000 West Street, 17th Floor
Wilmington, Delaware 19801
(302) 571-6600
kkeller@ycst.com

Attorneys for Defendants