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

DEFENDANTS' ANSWERING BRIEF IN OPPOSITION TO PLAINTIFFS' MOTION TO STRIKE PORTIONS OF DEFENDANTS' SUMMARY JUDGMENT BRIEF

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I. NATURE AND STAGE OF THE PROCEDINGS & SUMMARY OF ARGUMENT

To support its motion to strike, Allergan adopts a hypertechnical view of the Court's ruling that expressly permitted Alcon's written description summary judgment motion with respect to the '834 patent. Alcon has consistently alleged that there is no written description support for "about 0.15% (w/v)" in the claims of the '834 patent, and that fact is the basis for its written description summary judgment motion. Indeed, nowhere does the specification or original claims of the '834 patent teach that "about 0.15% (w/v)" of brimonidine tartrate will be "therapeutically effective" as the claims require. Alcon's position was amply summarized at the scheduling conference by its counsel:

> We simply want to look at the claim and specification and say there is no support for these claims because nothing in the claim relates to this [0.15% (w/v)] amount. Indeed, everything in the specification is 0.2 percent or higher, every chart, every example. It would only teach one to use that much. There is nothing there that would even suggest that you go to a lower amount.[1]

The statements made by Alcon and its counsel in interrogatory answers and during the scheduling conference, which are quoted in Allergan's opening brief, clearly emphasize that the 0.15% limitation is not supported by the specification of the '834 patent. The arguments in Alcon's motion are entirely consistent with these statements and stress, yet again, the lack of support for this same limitation. For example, in summarizing its section 112 defense, Alcon states:

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[1] Transcript of November 22, 2004 scheduling conference at 7, a copy of which is annexed hereto as Exhibit 1. The claimed concentration of active ingredient was an afterthought, added by amendment, only when Allergan realized that the claims of its pending application did not explicitly cover its newly-introduced commercial product, Alphagan®P, which coincidentally contains 0.15% (w/v) brimonidine tartrate.

> Neither the specification of the '834 patent nor any of the original disclosure (including the original 46 claims) in the Parent Application disclose the critical 0.15% limitation. There is nothing in the '834 patent's specification or original disclosure to establish that the inventors actually possessed such invention when they filed the provisional application from which priority is claimed. That fact alone mandates summary judgment.[2]

The 0.15% limitation is claimed as the amount of the active ingredient (brimonidine tartrate) needed for a "therapeutically effective" composition. If the specification of the '834 patent contained data as to therapeutic effectiveness, and if it showed, for instance, that 0.15% brimonidine tartrate was the threshold concentration to achieve therapeutic effectiveness, that would potentially be evidence of written description for the claim. However, no such data, and no commentary about concentrations necessary to achieve therapeutic effectiveness are included in the specification. Alcon is entitled to point that out to show that the dose-reduction claims ("up to about 0.15%") were made up after the fact and are wholly unsupported by the specification. Thus, the "therapeutically effective" preamble to the claims is entirely relevant to Alcon's argument that the '834 patent is invalid under section 112.

Allergan's arguments also ignore the applicable law on claim construction and, in effect, would require Alcon and this Court to ignore the alleged invention as actually claimed in the '834 patent as well as the prosecution history that explains the nature of that purported invention. Thus, in its brief, Alcon states:

> Moreover, since Allergan's attorneys repeatedly argued during prosecution of the '834 patent that a "therapeutically effective" formulation of brimonidine at this concentration ["up to about 0.15% (w/v)"] would have been "unexpected" and "surprising" and secured allowance on that very basis, Allergan cannot now argue that this "unexpected" finding would have been immediately

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[2] Defendants' Opening Brief In Support Of Their Motion For Summary Judgment Of Non-Infringement Of Allergan's U.S. Patent No. 6,673,337 And Invalidity Of Its U.S. Patent No. 6,641,834 ("Alcon Brief") at 18 (footnote omitted) (emphasis added) (D.I. 55).

> understood from the disclosure of the '834 patent, which lacks any pertinent teaching whatsoever. Accordingly, each claim of the '834 patent should be held invalid for failure to satisfy the written description requirement.[3]

Contrary to Allergan's accusations, Alcon's section 112 defense has not changed. Alcon has consistently asserted that the claims of the '834 patent are invalid because the claimed invention – a "therapeutically effective ophthalmic formulation" containing "up to 0.15% (w/v)" active ingredient – is not supported by the specification or the original claims. Allergan's attempt to dissect a claim into its individual limitations and interpret each one in isolation should be rejected.

II. ARGUMENT

A. Nature Of Allergan's Motion

The first sentence of Allergan's brief reads: "Allergan moves to strike Alcon's motion for summary judgment of non-infringement and invalidity to the extent it goes beyond the issues on which the Court gave Defendants permission to move for summary judgment."[4] Allergan, however, does not assert that Alcon's motion for summary judgment of non-infringement of the '337 patent violates the Scheduling Order. Moreover, Allergan does not seek to strike Alcon's motion for summary judgment on the '834 patent in its entirety. Allergan only seeks to strike (and thus prevent this Court from considering) all references to a critical limitation in each and every claim in the '834 patent, i.e., the requirement that the 0.15% (w/v) concentration of active

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3 Id. at 18-19 (emphasis in original).

4 Plaintiffs' Opening Brief In Support Of Their Motion To Strike Portions Of Defendants' Summary Judgment Brief ("Allergan Brief") at 1 (D.I. 68).

ingredient be "therapeutically effective."[5] Thus, even if Allergan's motion to strike were granted (which, of course, Alcon vigorously opposes), Alcon's motions for summary judgment would remain pending.

B. The Applicable Law Shows That Alcon's Interpretation Of The 0.15% Limitation Is Correct And That Its 35 U.S.C. § 112 Defense Has Not Changed

Allergan's unfounded accusations that the arguments in Alcon's motion for summary judgment violate the Scheduling Order appear to serve two purposes, neither of which should be condoned. First, it is clear that Allergan filed the instant motion in an attempt to divert the Court's attention from Alcon's summary judgment motion on the '834 patent. Second, Allergan characterized the alleged transgression, i.e., that Alcon "switched" its written description defense, as "litigation misconduct" and used that argument in its motion to pursue a charge of willful infringement.[6] In opposition, Alcon demonstrated that the summary judgment motion is fully consistent with the Scheduling Order and that Allergan's position is based upon a legally erroneous view of the principles of claim interpretation.[7]

In its summary judgment motion, Alcon emphasizes the lack of support for the 0.15% (w/v) limitation, which appears in all claims of the '834 patent. In so doing, Alcon quite properly references the claimed invention, which is a "therapeutically effective aqueous

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[5] Allergan also seeks to strike Alcon's "passing reference" to other invalidity defenses to the '834 patent. See Allergan Brief at 6. Alcon, however, is not pursuing these defenses at this time, and they were mentioned "in passing" merely to accentuate certain inconsistencies in Allergan's present position. As with its attempt to restrict the arguments presented in Alcon's court-authorized motion under section 112, Allergan wishes to prevent the Court from presenting Allergan's alleged invention and its '834 patent in proper context. Certainly, the Scheduling Order does not prohibit such presentation.

[6] See Letter Brief dated May 9, 2005, submitted to the Court by William J. Marsden (D.I. 64).

[7] See Letter Brief dated May 16, 2005, submitted to the Court by John W. Shaw (D.I. 75).

ophthalmic composition comprising . . . up to about 0.15% (w/v) [active ingredient] . . . ." (Claim 1). The 0.15% numerical limitation does not stand alone or in isolation, as Allergan argues. As Allergan's own expert witness, Dr. Valentino Stella, recognized, the 0.15% limitation is an integral part of the claimed "therapeutically effective" formulation and is viewed in the context of the surrounding claim language. See Declaration of Valentino Stella, Ph.D., at ¶¶ 18-19. Even Mr. Singer, counsel for Allergan, recognized that Alcon's defense focused on the "claimed invention." Thus, at the November 22, 2004 scheduling conference, he stated:

> [T]he issue on [the] written description claim is what in the specification discloses to one of ordinary skill whether the inventor was in possession of the claimed invention.[8]

Similarly, as Judge (now Chief Judge) Robinson succinctly observed in BOC Health Care, Inc. v. Nellcor, Inc., 892 F. Supp. 598, 613 (D. Del. 1995), aff'd, 98 F.3d 1357 (Fed. Cir. 1996) (non-precedential decision), "in reality, claim language must be construed as a whole and it is something of an intellectual fiction to separate the phrase of a claim as if they stood in isolation." Allergan ignores this holding and divorces the 0.15% limitation of active ingredient from the resulting "therapeutically effective" formulations containing that active ingredient.

The claims in the '834 patent all have the same preamble – "A therapeutically effective aqueous ophthalmic composition comprising . . . ." Allergan admits this is a claim limitation. Indeed, Allergan construes this limitation as "requir[ing] a therapeutically effective ophthalmic composition" having the additional limitations recited in the body of the claims.[9] Accordingly, Allergan has already conceded that the introductory language serves to "'give meaning to [the] claim and properly define the invention.'" Apple Computer, Inc. v. Articulate Systems, Inc., 234

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[8] See Transcript of November 22, 2004 scheduling conference at 21 (emphasis added), which is included as part of Exhibit 1.

F.3d 14, 22 (Fed. Cir. 2000), quoting In re Paulsen, 30 F.3d 1475, 1479 (Fed. Cir. 1994) (quoting DeGeorge v. Bernier, 768 F.2d 1318, 1322 n.3 (Fed. Cir. 1985)). This language cannot be ignored.

Allergan's argument that some "shift" has occurred in Alcon's position also mischaracterizes how claims are understood and, ultimately, Alcon's section 112 defense itself. The 0.15% (w/v) limitation on the concentration of active ingredient in the claimed formulations is not viewed in isolation, nor can it be divorced from the remainder of the claims. See Hockerson-Halberstadt, Inc. v. Converse, Inc., 183 F.3d 1369, 1374 (Fed. Cir. 1999) ("Proper claim construction, however, demands interpretation of the entire claim in context, not a single element in isolation." (emphasis added)); Middleton, Inc. v. Minnesota Mining and Manufacturing Co., 311 F.3d 1384, 1387 (Fed. Cir. 2002) ("As usual, the most important indicator of the meaning of [the disputed term] is its usage and context within the claim itself."). Thus, while the specific 0.15% (w/v) limitation is at the center of the present debate, "the context of the surrounding words of the claim" (e.g., "therapeutically effective") also "must be considered." Brookhill-Wilk 1 LLC v. Intuitive Surgical, Inc., 334 F.3d 1294, 1299 (Fed. Cir. 2003).[10]

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[9] See Joint Claim Chart at 5 (emphasis added), a copy of which is annexed hereto as Exhibit 2.

[10] During prosecution of the '834 patent, Allergan itself recognized that the 0.15% limitation could not be read in isolation, but was one facet of the claimed invention: "The current claims are directed to therapeutically effective aqueous ophthalmic compositions comprising brimonidine and salts and esters thereof at a pH of up to about 7.0, and in a concentration of about 0.15% or less." See Prosecution History of the '834 patent, Reply to Office Action mailed on March 17, 2003 at 4, a copy of which is annexed hereto as Exhibit 3. (emphasis added).

C. Alcon's Preliminary Views On Claim Construction Are Irrelevant To Its Final Position Set Forth In The Joint Claim Chart

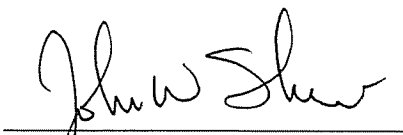
As one last attempt to show Alcon's "shift" in position, Allergan notes that Alcon originally contended that the claim term "about 0.15% "should be interpreted as "0.1499-0.1501%." According to Allergan, after an Alcon witness was deposed, Alcon abandoned that claim construction and asserted a "new" written description defense. This argument, which Allergan also made to support its charge of willful infringement, is simply wrong. The ultimate interpretation of the term "about 0.15% (w/v)" has no effect whatsoever on Alcon's section 112 defense. Moreover, during preparation of the Joint Claim Chart, Alcon initially proposed a limited range for the "about 0.15% (w/v)" limitation. After exchanging preliminary positions with Alcon and following the joint meet-and-confer conference mandated by the Scheduling Order, Alcon submitted its final position on claim interpretation, which was included in the Joint Claim Chart. (See Exhibit 2). For Allergan to rely on this preliminary claim interpretation without explicitly informing this Court of the circumstances is outrageous. Nevertheless, the precise numerical range used to construe the term "about 0.15% (w/v)" is entirely irrelevant to Alcon's written description defense, because the specification supplies no teaching or support to suggest that any particular concentration of active ingredient was Allergan's invention. Thus, once again Allergan has failed to show that Alcon changed its position or that its summary judgment motion violates the terms of the Scheduling Order.

III. CONCLUSION

For the reasons set forth herein, Allergan's motion to strike should be denied.

Respectfully submitted,

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Dated: May 23, 2005

EXHIBIT 1

IN THE UNITED STATES DISTRICT COURT
IN AND FOR THE DISTRICT OF DELAWARE

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

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Wilmington, Delaware
Monday, November 22, 2004
2:00 p.m.
In Chambers

- - -

BEFORE: HONORABLE GREGORY M. SLEET, U.S.D.C.J.

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specification. They immediately canceled all the claims by way of preliminary amendment, put in new claims. The new claims have an upper limit on the amount of the active ingredient in the product. This product was previously sold at .2 percent, and when they canceled the claims they put a limit in and they claimed the use of the product with up to .15 percent. There is not a word in the specification that mentions .15 percent. There is not a word in the specification that mentions an upper limit.

So we have a straightforward lack of written description, invalidity based on absence of written description, requires no discovery whatsoever. The only issue is looking at the specification, does that specification support the revised claims which added the new matter of up to .15 percent.

So in the case of the continuation patent, it is a written description summary judgment argument. No discovery required. We simply want to look at the claim and spec and say there is no support for these claims because nothing in the claim relates to the amount. Indeed, everything in the specification is .2 percent or higher, every chart, every example. It would only teach one to use that much. There is nothing there that would even suggest that you go to a lower amount.

In the first patent, where we have the issue of

It is an ANDA issue lawsuit. There is no money at issue. It is a right to get on the marketplace. It will before you as a finder of fact, but you may decide at this stage of the case, as a matter of law, this can only go one way because there is not support in the spec for the up to, the limitation of up to .15 percent.

If it's a disputed fact, you deny the summary judgment motion. But the Federal Circuit says you can do this. The Rochester case says absolutely.

THE COURT: I understand. But your opponent suggests that the Court is going to need to hear from experts on this particular point. You say no.

MR. THOMASCH: Absolutely not. Whether it is there or not the Court can gather by reading the specification.

THE COURT: Why can't I read the specification and simply resolve the issue?

MR. SINGER: The issue on a written description claim is what in the specification discloses to one of ordinary skill whether the inventor was in possession of the claimed invention. Mr. Thomasch says that there is not a word there. And the limitation is about .15. That's what we are talking about, is a limitation of about .15 in some of the dependent claims. Again, I pointed here today to something that is .1451 that I think notifies someone of

EXHIBIT 2

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

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

JOINT CLAIM CHART

'337 Patent

Asserted Claim	**Agreed Upon Construction**	**Allergan's Proposed Construction**	**Alcon's Proposed Construction**
Claim 1			
1. A therapeutically effective ophthalmic composition comprising:	The claim requires a therapeutically effective ophthalmic composition, and the term "therapeutically effective" is used in its ordinary sense.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
an alpha-2-adrenergic agonist component in an amount effective to provide a therapeutic benefit to a patient in whom the composition is administered; and	The claimed composition must contain an alpha-2-adrenergic agonist component in an amount that is effective to provide a therapeutic benefit to a patient.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
a solubility enhancing component other than a cyclodextrin	The parties dispute the construction of this limitation.	The claimed composition contains a solubility	The claimed composition must contain an anionic component, other than a cyclodextrin, in an

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
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.		enhancing component, which is a component that enhances the solubility of the alpha-2-adrenergic agonist component, and any solubility enhancing component other than a cylclodextrin is covered by the claim. The solubility enhancing component must be present in such an amount that the solubility of the alpha-2-adrenergic agonist component in the composition is increased relative to its solubility in a similar composition without the solubility enhancing component. Support for proposed construction: '337 patent, abstract, col. 2, lines 13-20, col. 4, lines 60-65, col. 6, lines 17-41, '337 patent file history, Reply to Office Action, Dated June 16, 2003.	amount effective to increase the solubility of the alpha-2-adrenergic agonist component in the composition relative to the solubility of the alpha-2-adrenergic agonist component in an otherwise identical composition without the anionic component. In addition, the "solubility enhancing component" cannot be polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers or hydroxymethylcellulose. Support for proposed construction: Application No. 09/904,018 (parent application of the application which issued as the '337 patent): Office Action mailed September 18, 2002; Response to Restriction Requirement received by PTO on October 22, 2002; Office Action dated January 9, 2003; Interview Summary, mailed 3/3/03; Reply to Office Action, received by the PTO March 17, 2003 including Declaration of Orest Olejnik; '337 patent, Office Action, mailed March 13, 2003; Reply to Office Action, dated June 16, 2003.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
Claim 2			
2. The composition of claim 1 wherein the alpha-2-adrenegic component is selected from the group consisting of imino-imidazolines, imidazolines, imidazoles, azepines, thiazines, oxazolines, guanidines, catecholamines, derivatives thereof, and mixtures thereof.	Claim 2 contains all the limitations of claim 1, with the additional requirement that the alpha-2-adrenergic agonist component must be: an imino-imidazoline, imidazoline, imidazole, azepine, thiazine, oxazoline, guanidine, catecholamine, derivative of one of the foregoing, or a mixture of one of the foregoing.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 3			
3. The composition of claim 1 wherein the therapeutically active component includes a quinoxaline component.	Claim 3 includes all the limitations of claim 1, with the further requirement that the composition must contain a quinoxaline component.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 4			
4. The composition of claim 3 wherein the quinoxaline component is selected from the group consisting of quinoxaline, derivatives thereof, and mixtures thereof.	Claim 4 includes all the limitations of claims 1 and 3, with the further requirement that the quinoxaline component must be a quinoxaline, a derivative of quinoxaline, or mixture of two or more of the foregoing.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
Claim 6			
6. The composition of claim 1 wherein the solubility enhancing component is effective to increase the solubility in a biological environment of the alpha-2-adrenergic agonist component relative to the solubility in a biological environment of an identical alpha-2-adrenergic agonist component in a similar composition without the solubility enhancing component.	The parties dispute the construction of this limitation.	Claim 6 includes all the limitations of claim 1, with the further requirement that the solubility enhancing component is effective to increase the solubility in a biological environment of the alpha-2-adrenergic agonist component relative to its solubility in a similar composition without the solubility enhancing component. Support for proposed construction: '337 patent, col. 1, lines 58-64, col. 4, lines 41-47.	Claim 6 contains all the limitations of claim 1, with the further requirement that the "solubility enhancing component" must be effective to increase the solubility in a biological environment of the alpha-2-adrenergic agonist component relative to the solubility in the same biological environment of the alpha-2-adrenergic agonist component in an otherwise identical composition without the "solubility enhancing component." Support for proposed construction: As relevant to the construction of claim 6, Alcon incorporates its comment to claim 1.
Claim 9			
The composition of claim 1 which further comprises an effective amount of a preservative.	Claim 9 includes all the limitations of claim 1 with the further requirement that the composition must contain a component that assists in the preservation of the composition.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
Claim 10			
The composition of claim 6 which further comprises an effective amount of a preservative.	Claim 10 includes all the limitations of claim 6 with the further requirement that the composition must contain an effective amount of a component that assists in the preservation of the composition.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.

'834 Patent

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
Claim 1			
1. A therapeutically effective aqueous ophthalmic composition comprising:	The claim requires a therapeutically effective ophthalmic composition, and the term "therapeutically effective" is used in its ordinary sense.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate,	The parties dispute the construction of this limitation.	The claimed composition contains up to approximately 0.15% (w/v) brimondine tartrate. Support for proposed construction: The term "about" is used in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, col. 1, lines 33-53, col. 2, lines 48-52, col. 3, lines 23-36, col. 6, lines 8-16, col. 11, lines 1-6,	The claimed composition must contain up to 0.155% (w/v) (the upper limit of 0.15 ± 0.005% (w/v)) of brimondine tartrate. The specification (including the claims as originally filed) and prosecution history of the '834 patent only reflect testing of brimonidine tartrate solutions at concentrations of 0.5% (w/v) and 0.2% (w/v) and thus provide no teaching or

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		Example 2 and descriptive text, Table IV and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834 patent file history, Reply to Office Action, dated Mar. 24, 2003.	guidance supporting the terms "up to about 0.15% (w/v)," "up to 0.15% (w/v)," or "about 0.15% (w/v)" nor do they disclose that such compositions are within the scope of the alleged invention. In *Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005), the court rejected the patentee's attempt to define the terms "about 70 mg" and "about 35 mg" as limited to the precise numerical values disclosed, without any surrounding range. Thus, in order to supply a range, but in light of the absence of any teaching in the specification as guidance for the same, Alcon proposes that the term "about" be interpreted to encompass the full range of values that would normally be rounded up or down to 0.15%.
the composition having a pH of about 7.0 or greater,	The parties dispute the construction of this limitation.	The claimed composition has a pH of approximately 7.0 or greater. Support for proposed construction: The term "about" is used	The composition must have a pH of 6.95 (the lower limit of 7.0 $\pm$ 0.05) or greater. The specification (including the

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, col. 4, lines 22-33, col. 11, lines 1-6, Example 2 and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834 patent file history, Reply to Office Action, dated Mar. 24, 2003.	claims as originally filed) and the prosecution history of the '834 patent provide no teaching regarding the scope of the pH 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 pH 7.0.
and the 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate being soluble in the composition at about 21° C.	The parties dispute the construction of this limitation.	The brimonidine tartrate must be soluble in the composition at approximately 21° C. Support for proposed construction: The term "about" is used in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, Example 2 and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834	The brimondine tartrate must be soluble in the composition at 21 ± 0.5C The specification (including the claims as originally filed) and the prosecution history of the '834 patent provide no 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.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		patent file history, Reply to Office Action, dated Mar. 24, 2003.	
Claim 2			
2. The composition of claim 1 which includes up to 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate.	Claim 2 includes all the limitations of claim 1, with the additional requirement that the composition must include up to 0.15% (w/v) brimonidine tartrate.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 3			
3. The composition of claim 1 which includes about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate.	The parties dispute the construction of this limitation.	Claim 3 includes all the limitations of claim 1, with the additional requirement that the composition must include approximately 0.15% brimonidine tartrate. Support for proposed construction: The term "about" is used in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, col. 1, lines 33-53, col. 2, lines 48-52, col. 3, lines 23-36, col. 6, lines 8-16, col. 11, lines 1-6, Example 2 and descriptive text, Table IV and descriptive text, Application No. 09/904,018 (parent application of the application which	Claim 3 contains all the limitations of claim 1, with the additional requirement that the composition must include 0.15% ± 0.005% (w/v) brimondine tartrate. Support for proposed construction: As relevant to the construction of claim 3, Alcon incorporates its comments to claim 1.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		issued as the '834 patent, including the original claims), '834 patent file history, Reply to Office Action, dated Mar. 24, 2003.	
Claim 4			
4. The composition of claim 1 which included 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate.	Claim 4 includes all the limitations of claim 1, with the additional requirement that the composition must include 0.15% (w/v) brimonidine tartrate.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 5			
5. The composition of claim 1 having a pH of 7.0 or greater.	Claim 5 includes all the limitations of claim 1, with the additional requirement that the pH of the composition must be 7.0 or greater.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 6			
6. The composition of claim 1 which further comprises a preservative selected from the group consisting of an oxy-chloro component and a quaternary ammonium compound in an amount effective to at least assist in preserving the composition.	Claim 6 includes all the limitations of claim 1 and further requires that the composition must contain either an oxy-chloro or quaternary ammonium preservative in an amount effective to assist in preserving the composition.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 8			
8. The composition of claim 1 which is substantially free of anionic cellulosic derivatives.	Claim 8 includes all the limitations of claim 1 and further requires that the composition is	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
	substantially free of anionic cellulosic derivatives.		
Claim 9			
The composition of claim 1 which is substantially free of carboxymethyl cellulose.	Claim 9 includes all the limitations of claim 1 and further requires that the composition is substantially free of carboxymethyl cellulose.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 10			
10. A therapeutically effective aqueous ophthalmic composition comprising:	The claim requires a therapeutically effective ophthalmic composition, and the term "therapeutically effective" is used in its ordinary sense.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
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 parties dispute the construction of this limitation.	The claimed composition contains up to approximately 0.15% (w/v) brimondine, salts of brimonidine, esters of brimonidine, or mixtures of the foregoing. Support for proposed construction: The term "about" is used in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). See also '834 patent, Figure 1, col. 1, lines 33-53, col. 2, lines 48-52, col. 3, lines 23-36, col. 6, lines 8-16, col. 11, lines 1-6, Example 2 and	The claimed composition must contain up to 0.155% (w/v) (the upper limit of 0.15 ± 0.005% (w/v)) of brimondine, salts of brimonidine, esters of brimonidine, or mixtures of two or more of the foregoing. The specification (including the claims as originally filed) and prosecution history of the '834 patent only reflect testing of brimonidine tartrate solutions at concentrations of 0.5% (w/v) and 0.2% (w/v) and thus provide no teaching or

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		descriptive text, Table IV and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834 patent file history, Reply to Office Action, dated Mar. 24, 2003.	guidance supporting the terms "up to about 0.15% (w/v)," "up to 0.15% (w/v)," or "about 0.15% (w/v)" nor do they disclose that such compositions are within the scope of the alleged invention. In *Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005), the court rejected the patentee's attempt to define the terms "about 70 mg" and "about 35 mg" as limited to the precise numerical values disclosed, without any surrounding range. Thus, in order to supply a range, but in light of the absence of any teaching in the specification as guidance for the same, Alcon proposes that the term "about" be interpreted to encompass the full range of values that would normally be rounded up or down to 0.15%.
the composition having a pH of about 7.0 or greater,	The parties dispute the construction of this limitation.	The claimed composition has a pH of approximately 7.0 or greater. Support for proposed construction: The term "about" is used	The claimed composition must have a pH of 6.95 (the lower limit of 7.0 ± 0.05) or greater. The specification (including the

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, col. 4, lines 22-33, col. 11, lines 1-6, Example 2 and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834 patent file history, Reply to Office Action, dated Mar. 24, 2003.	claims as originally filed) and the prosecution history of the '834 patent provide no teaching regarding the scope of the pH 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 pH 7.0.
and the component being soluble in the composition at about 21° C.	The parties dispute the construction of this limitation.	The brimonidine tartrate must be soluble in the composition at approximately 21° C. Support for proposed construction: The term "about" is used in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, Example 2 and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834 patent file history,	The component must be soluble in the composition at 21 ± .5°C. The specification (including the claims as originally filed) and the prosecution history of the '834 patent provide no 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.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		Reply to Office Action, dated Mar. 24, 2003.	
Claim 11			
11. The composition of claim 10 which includes up to 0.15% (w/v) of the component.	Claim 11 includes all the limitations of claim 10, with the additional requirement that the composition must include up to 0.15% (w/v) of the component selected from the group described in claim 10.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 12			
12. The composition of claim 10 which includes about 0.15% (w/v) of the component	The parties dispute the construction of this limitation.	Claim 12 includes all the limitations of claim 10, with the additional requirement that the composition must include approximately 0.15% (w/v) of the component selected from the group described in claim 10. Support for proposed construction: The term "about" is used in its ordinary sense, meaning "approximately." *See Merck & Co. v. Teva Pharms., Inc.*, 395 F.3d 1364 (Fed. Cir. 2005). *See also* '834 patent, Figure 1, col. 1, lines 33-53, col. 2, lines 48-52, col. 3, lines 23-36, col. 6, lines 8-16, col. 11, lines 1-6, Example 2 and descriptive text.	The claimed composition must include all the limitations of claim 10, with the additional requirement that the composition must include 0.15 ± 0.005% (w/v) of the component listed in claim 10. As relevant to the construction of claim 12, Alcon incorporates its comments to claim 10.

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
		Table IV and descriptive text, Application No. 09/904,018 (parent application of the application which issued as the '834 patent, including the original claims), '834 patent file history, Reply to Office Action, dated Mar. 24, 2003.	
Claim 13			
13. The composition of claim 10 which includes 0.15% (w/v) of the component	Claim 13 includes all the limitations of claim 10, with the additional requirement that the composition must include 0.15% (w/v) of the component selected from the group described in claim 10.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 14			
14. The composition of claim 10 having a pH of 7.0 or greater.	Claim 14 includes all the limitations of claim 10, with the additional requirement that the pH of the composition must be 7.0 or greater.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 17			
17. The composition of claim 10 which is substantially free of anionic cellulosic derivatives.	Claim17 includes all the limitations of claim 10 and further requires that the composition is substantially free of anionic cellulosic derivatives.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.
Claim 18			
18. The composition of claim 10 which is	Claim 18 includes all the limitations of claim 10 and further	The parties do not dispute the construction of this	The parties do not dispute the construction of this

Asserted Claim	Agreed Upon Construction	Allergan's Proposed Construction	Alcon's Proposed Construction
substantially free of carboxymethyl cellulose.	requires that the composition is substantially free of carboxymethyl cellulose.	limitation.	limitation.
Claim 20			
20. The composition of claim 10 which further comprises a preservative selected from the group consisting of an oxy-chloro component and a quaternary ammonium compound in an amount effective to at least assist in preserving the composition.	Claim 20 includes all the limitations of claim 10 and further requires that the composition must contain either an oxy-chloro or quaternary ammonium preservative in an amount effective to assist in preserving the composition.	The parties do not dispute the construction of this limitation.	The parties do not dispute the construction of this limitation.

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EXHIBIT 3

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of Olejnik, et al.	Group Art Unit: 1615
Serial No: 10/236,566	Examiner: Bennett, R.
Filed: September 6, 2002	
For: COMPOSITIONS CONTAINING ALPHA-2-ADRNERGIC AGONIST COMPONENTS	

REPLY TO OFFICE ACTION

This communication is in Reply to the Office Action mailed December 18, 2001. Applicants have carefully studied the Office Action, and respectfully request reconsideration of the claim rejections in light of the claim amendments and comments which follow.

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AMENDMENTS TO THE CLAIMS

Kindly make the following amendments to the claims:

R1 C1 — 47. (Amended) A therapeutically effective aqueous ophthalmic composition comprising:
~~water; and~~
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-ylamino) quinoxaline tartrate being soluble in the composition at about 21°C.

48-52 Original Claims

R2 — 53. (Amended) The composition of claim 47 which further comprises a preservative selected from the group consisting of an oxy-chloro component and a quaternary ammonium compound in an amount effective to at least assist in preserving the composition.

54-56 Original Claims

R3 C2 — 57. (Amended) A therapeutically effective aqueous ophthalmic composition comprising:
~~water; and~~
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.

58-66 Original Claims

R4 — 67. (New) The composition of claim 55 in which the preservative comprises benzalkonium chloride.

68. (New) The composition of claim 57 which further comprises a preservative selected from the group consisting of an oxy-chloro component and a quaternary ammonium compound in an amount effective to at least assist in preserving the composition.

69. (New) The composition of claim 68 in which the preservative comprises benzalkonium chloride.

70. (New) The composition of claim 68 in, which the preservative comprises a oxy-chloro component.

REMARKS

Applicants would like to thank Examiner Bennett for her courtesy in granting and conducting a telephonic interview on February 25, 2003. During the interview Examiner Bennett and the undersigned discussed the outstanding rejections and proposed claim amendments.

Independent claims 47 and 57 and dependent claim 53 have been amended, and new claims 67-70 added. All the amendments are supported by the specification. Claims 47 and 57 were amended to indicate that what is being claimed is a therapeutically effective aqueous ophthalmic composition. Support for this amendment can be found, e.g., at page 1, lines 15-16 and page3-7. Claim 52 was amended to add a Markush group of preservative components including oxy-chloro compounds and quaternary ammonium compounds; see pages 18-20. The new claims provide specific embodiments of the invention.

Applicants would like to point out that these claim amendments and cancellations have been made solely in order to enable early allowance of certain aspects of the invention; Applicants have amended claims in this application with the understanding that they may reserve the right to present the unamended versions thereof in a subsequent patent application.

Provisional Double Patenting

The Examiner has made a provisional double patenting rejection of the invention claimed in this patent application over co-pending patent application Serial No. 09/904,018. Applicants are herewith filing a Terminal Disclaimer over the '018 application; thus Applicant believe this rejection is now moot

35 USC §103

The Examiner rejected claims 47-66 as being unpatentable pursuant to 35 USC §103 over Burke (US 5,215,991). Although not explicitly stated, Applicants infer that this rejection is in view of Beck (US Patent 6,358,935), since the discussion mentions the Beck patent. If Applicants are in error, correction is respectfully sought. The Examiner has stated that Burke discloses brimonidine (5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline) in various formulations and concentrations, including an aqueous formulation; the Examiner also states that Beck discloses cyclodextrin-containing compositions containing an oxy-chloro component. The Examiner argues that the currently claimed invention is the result of routine optimization of the conditions cited in Burke. Moreover, the Examiner has cited Beck for the disclosure of oxy-chloro preservatives therein, notwithstanding these preservatives are disclosed as for use with cyclodextrins, which not elements of the compositions presently claimed. Applicants respectfully traverse this rejection for the following reasons.

The current claims are directed to therapeutically effective aqueous ophthalmic compositions comprising brimonidine and salts and esters thereof at a pH of up to about 7.0, and in a concentration of about 0.15% or less. Other claims indicate that the composition is preserved using a quaternary ammonium preservative or an oxychloro preservative.

To appreciate the surprising aspects of the present invention it is important to understand that previous 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). This formulation was approved for marketing in the United States and foreign countries under the trade name Alphagan®.

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. As such, a greater amount of the active drug is able to enter the cornea of the eye at a given solution concentration; this effect counters the effects of decreased brimonidine solubility at the higher pH. See specification at e.g., paragraph bridging pages 1 and 2.

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.

For the Examiner's convenience, Applicants hereby attach a copy of an article Katz, et al., *J. Glaucoma* 11:119 (April 2002) which shows the comparison of the 0.2% brimonidine formulation having a pH 6.3-6.5 (the "0.2% formulation") with 0.15% brimonidine solution at pH 7.2 (the 0.15% formulation).

Although the Katz paper does not disclose the pH of either solution, Applicants hereby enclose a Declaration of Amy Batoosingh, Director of Ophthalmological Clinical Research at Allergan, Inc. Ms. Batoosingh, whose work is contained within and acknowledged on page 126 of Katz, indicates in her Declaration that the formulation called "brimonidine 0.2%" in the Katz paper, which used benzalkonium chloride as a preservative, comprised 0.2% brimonidine at pH 6.3-6.5, and that the formulation termed "brimonidine-Purite 0.15%" in Katz, (which used oxy-chloro as a preservative) comprised 0.15% brimonidine at pH 7.2.

As can be seen in Figure 1 on page 122 of Katz, topical application of the 0.15% formulation resulted in no statistically significant differences in its ability to lower intraocular pressure (IOP) compared to the 0.2% formulation, despite 25% less active agent in the former formulation. Thus,

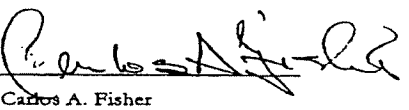
lowering the concentration, when the pH is above about 7.0 unexpectedly had no significant effect on therapeutic efficacy, when compared to the 0.2% formulation.

The advantages of this invention are manifest. Among others, it can be seen that although ophthalmic hypotensive therapeutic efficacy of the 0.15% solution is the same as for the 0.2% solution, the reduced concentration (and thus the reduced dosage) results in a lower potential for systemic side effects, which are typically caused by drainage of topically applied drugs from the eye to the stomach through the nasolacrimal duct. Although brimonidine's side effects are not as severe as some other glaucoma medications, they can still include sedation, hypotension, and reduction in heat rate in some patients. A reduction in the dosage by 25% reduces the likelihood and severity of such side-effects.

Thus, 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 brimonidine, and to the pKa of the compound.

For this reason it can be seen that these results were completely unforeseen and surprising, and could therefore not have been anticipated by a person of skill in the art. For this reason, Applicants respectfully request reconsideration and withdrawal of the outstanding rejection, and ask the Examiner to permit the claims to proceed to issue. Should there be any fee in connection with this communication, the Director is authorized to use the Applicants' Deposit Account 01-0885 for the payment of such fees.

Respectfully submitted,

By: 

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CERTIFICATE OF SERVICE

I, Karen E. Keller, Esquire hereby certify that on May 23, 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:

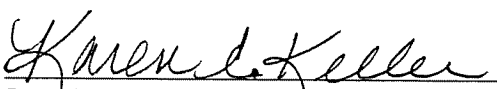
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I further certify that on May 23, 2005, I caused a copy of the foregoing document to be served by hand delivery on the above-listed counsel of record and on the following non-registered participants in the manner indicated:

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