EXHIBIT A

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

FIRST AMENDED ANSWER AND COUNTERCLAIMS

Defendants, Alcon Inc., Alcon Laboratories, Inc. and Alcon Research Ltd. (collectively "Alcon"), for their Amended Answer to the Complaint filed by Allergan, Inc. and Allergan Sales, LLC. (collectively "Allergan"), state as follows:

The Nature of the Action

1. Alcon admits that paragraph 1 of the Complaint alleges infringement of United States Patents Nos. 6,641,834 ("the '834 patent") and 6,673,337 ("the '337 patent").

The Parties

2. Alcon admits the allegations of paragraph 2 of the Complaint.

3. Alcon admits the allegations of paragraph 3 of the Complaint.

4. Alcon admits the allegations of paragraph 4 of the Complaint.

Jurisdiction and Venue

5. Alcon admits the allegations of paragraph 5 of the Complaint.

6. Alcon admits the allegations of paragraph 6 of the Complaint.

Background

7. Alcon admits that the '834 patent reflects that such patent, entitled "Compositions Containing Alpha-2-Adrenergic Agonist Components," issued to Orest Olejnik and Edward D.S. Kerslake on November 4, 2003, but denies that a true and accurate copy of same is annexed to the Complaint as Exhibit A as alleged in paragraph 7 of the Complaint.

8. Alcon lacks knowledge or information sufficient to form a belief as to the truth of the allegations in paragraph 8 of the Complaint and therefore denies such allegations.

9. Alcon admits that the '337 patent reflects that such patent, entitled "Compositions Containing Alpha-2-Adrenergic Agonist Components," issued to Orest Olejnik and Edward D.S. Kerslake on January 6, 2003, and that a copy of same is annexed to the Complaint as Exhibit B as alleged in paragraph 9 of the Complaint.

10. Alcon lacks knowledge or information sufficient to form a belief as to the truth of the allegations in paragraph 10 of the Complaint and therefore denies such allegations.

11. Alcon admits the allegations of paragraph 11 of the Complaint.

12. Upon information and belief, Alcon admits that ALPHAGAN®P is encompassed within the scope of at least one claim of the '834 patent and at least one claim of the '337 patent.

13. Alcon lacks knowledge or information sufficient to form a belief as to the truth of the allegation that pediatric exclusivity was granted on December 20, 2001, and therefore denies such allegation, but admits the remaining allegations of paragraph 13 of the Complaint.

14. Alcon admits the allegations of paragraph 14 of the Complaint.

15. Alcon admits the allegations of paragraph 15 of the Complaint.

Count I

16. Alcon repeats and realleges the responses to the allegations in paragraphs 1 through 15 hereof as though fully set forth herein.

17. Alcon denies that it has committed an act of infringement under 35 U.S.C. §271(e)(2) by submitting NDA No. 21-764 or otherwise, but admits that Alcon submitted NDA No. 21-764 to the FDA under 505(b)(2) of the FDCA to obtain approval to engage in the commercial manufacture and sale of its proposed Brimonidine Tartrate Ophthalmic Solution 0.15% product.

18. Alcon denies the allegations of paragraph 18 of the Complaint.

19. Alcon denies the allegations of paragraph 19 of the Complaint.

Count II

20. Alcon repeats and realleges the responses to the allegations in paragraphs 1 through 15 hereof as though fully set forth herein.

21. Alcon denies that it has committed an act of infringement under 35 U.S.C. §271(e)(2) by submitting NDA No. 21-764 or otherwise, but admits that Alcon submitted NDA No. 21-764 to the FDA under section 505(b)(2) of the FDCA to obtain approval to engage in the commercial manufacture and sale of its proposed Brimonidine Tartrate Ophthalmic Solution 0.15% product.

22. Alcon denies the allegations of paragraph 22 of the Complaint.

23. Alcon denies the allegations of paragraph 23 of the Complaint.

AFFIRMATIVE DEFENSES

Alcon, for its affirmative defenses to the allegations in Counts I and II of the Complaint, alleges as follows:

First Affirmative Defense

24. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claim of the '834 patent, literally or under the doctrine of equivalents.

Second Affirmative Defense

25. Allergan is estopped from asserting that Alcon will infringe any claims of the '834 patent due to the amendments, arguments and other statements made by or on behalf of applicants during prosecution before the United States Patent and Trademark Office of the applications resulting in issuance of such patent.

Third Affirmative Defense

26. The '834 patent is invalid for failure to comply with one or more requirements of Title 35, United States Code, sections 102, 103, 112, and/or 256.

Fourth Affirmative Defense

27. The '834 patent is unenforceable because, as described in the counterclaims section below, during prosecution of one or more applications related to the '834 patent, person(s) charged with a duty of candor and good faith before the United States Patent and Trademark Office failed to discharge that duty and engaged in inequitable conduct.

Fifth Affirmative Defense

28. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claim of the '337 patent, literally or under the doctrine of equivalents.

Sixth Affirmative Defense

29. Allergan is estopped from asserting that Alcon's proposed brimonidine product will infringe any claims of the '337 patent due to the amendments, arguments and other

statements made by or on behalf of applicants during prosecution before the United States Patent and Trademark Office of the applications resulting in issuance of such patent.

Seventh Affirmative Defense

30. The '337 patent is invalid for failure to comply with one or more requirements of Title 35, United States Code, sections 102, 103 and/or 112.

Eighth Affirmative Defense

31. The '337 patent is unenforceable because, as described in the counterclaims section below, during prosecution of one or more applications related to the '337 patent, person(s) charged with a duty of candor and good faith before the United States Patent and Trademark Office failed to discharge that duty and engaged in inequitable conduct.

Ninth Affirmative Defense

32. Upon information and belief, Allergan is barred from recovery pursuant to the doctrine of unclean hands as described in the counterclaims section below.

COUNTERCLAIMS

Alcon, for its counterclaims herein against Allergan, alleges as follows:

Nature of the Action

33. This is an action for a judgment declaring United States Patent Nos. 6,641,834 (the "'834 patent") and 6,673,337 (the "'337 patent") invalid, not infringed, and unenforceable.

The Parties

34. Alcon Laboratories, Inc. is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 6201 South Freeway, Forth Worth, Texas.

35. Alcon Research, Ltd. is a limited partnership organized and existing under the laws of the state of Texas and has its principal place of business in Fort Worth, Texas.

36. Alcon, Inc. is a corporation organized and existing under the laws of Switzerland and has its principal place of business in Hunenberg, Switzerland.

37. Allergan, Inc. is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 2525 Dupont Drive, Irvine, California.

38. Allergan Sales, LLC. is a limited liability company organized and existing under the laws of the State of Delaware and has its principal place of business at 2525 Dupont Drive, Irvine, California.

Jurisdiction and Venue

39. This court has subject matter jurisdiction over this action under the Declaratory Judgment Act and the Patent Laws of the United States, more particularly under Title 28, U.S.C. sections 2201 and 2202 and Title 35, U.S.C. section 1 *et seq.* An actual case or controversy exists between Alcon and Allergan as to the validity, infringement, and enforceability of the '834 and '337 patents, as evidenced by the Complaint and Answer in this action.

40. Venue is proper in this Court pursuant to Title 28, U.S.C. sections 1391(b) and (c).

Factual Background

41. The patents most relevant to this suit include:

a. U.S. Patent No. 6,627,210 (hereinafter "the '210 patent"), which issued on or about September 30, 2003. The '210 patent claims, *inter alia*, a therapeutically effective aqueous composition comprising a 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, or a salt or ester thereof, in a therapeutically effective amount and a polyanionic solubility enhancing component.

b. U.S. Patent No. 6,641,834 (hereinafter "the '834 patent"), which issued on or about November 4, 2003. The '834 patent claims, *inter alia*, a therapeutically effective aqueous ophthalmic composition having a pH of about 7.0 or greater comprising up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate being soluble in the composition at about 21°C.

c. U.S. Patent No. 6,673,337 (hereinafter "the '337 patent"), which issued on or about January 6, 2004. The '337 patent claims, *inter alia*, a therapeutically effective ophthalmic composition comprising an alpha-2-adrenergic agonist component other than a cyclodextrin in a therapeutically effective amount and a solubility enhancing component.

42. The '834 and '337 patents both claim benefit to Application Serial No. 09/904,018 ("the Parent Application"), which matured into the '210 patent. The '834 patent matured from a continuation application of the Parent Application. The '337 patent matured from a divisional application of the Parent Application.

43. The '210, '834 and '337 patents contain the same specification (but for, understandably, differences in the claims and the section entitled "Cross Reference to Related Application").

44. The '210, '834 and '337 patents each claim therapeutically effective compositions.

45. The '210, '834 and '337 patents each name Orest Olejnik and Edward D.S. Kerslake as their inventors, who are, and/or were, employed by Allergan.

46. The '210, '834 and '337 patents were each prosecuted by, or on behalf of, Allergan.

47. The '210, '834 and '337 patents were each examined by Rachel M. Bennett (hereinafter "Patent Examiner") for the United States Patent and Trademark Office (hereinafter "PTO").

48. During prosecution of the applications that matured into '210, '834 and '337 patents, each claim of each application was rejected as obvious under 35 U.S.C. § 103 over, *inter alia*, the prior art Burke reference (United States Patent No. 5,215,991) and subsequently amended prior to issuance.

49. Carlos A. Fisher, then an Allergan employee, was an attorney of record in connection with the prosecution of the applications that matured into the '210, '834 and '337 patents on behalf of Allergan after the claims in those applications were rejected over Burke.

50. Allergan has alleged that Alcon infringes the '834 and '337 patents.

51. Allergan does not allege that Alcon infringes the '210 patent.

Allergan's Procurement of the '210, '834 and '337 Patents By Inequitable Conduct

52. The subject matter and prosecution of the '210, '834 and '337 patents are intertwined.

53. Allergan filed the Parent Application, which matured into the '210 patent, on July 21, 2001. That application, naming Orest Olejnik as the first inventor, claimed, *inter alia*, a composition comprising an alpha-2-adrenergic agonist in a therapeutically effective amount and a solubility enhancing component.

54. The application that matured into the '834 patent was filed on September 6, 2002. That application was accompanied by a Preliminary Amendment that cancelled all pending claims and added claims to a composition containing, *inter alia*, "up to about 0.15% (w/v)" of brimonidine tartrate.

55. The application that matured into the '337 patent was filed on November 19, 2002, as a divisional application of the Parent Application, and was directed to compositions containing an oxy-chloro preservative. The application was accompanied by a Preliminary Amendment that cancelled all pending claims and added claims to a composition containing, *inter alia*, an alpha-2-adrenergic agonist in a therapeutically effective amount and an oxy-chloro preservative component.

56. In the only Office Action during prosecution of the '834 patent, mailed on December 18, 2002, the Examiner rejected all pending claims as obvious over the Burke (U.S. Patent No. 5,215,991) in view of Beck et al. (U.S. Patent No. 6358935). The Patent Examiner noted that Burke disclosed: (1) the claimed compound, 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, among its most preferred alpha-2-adrenergic compounds; (2) at a concentration from about 0.001% to about 1.0% (w/v), which encompassed the concentration range in the claims ("up to about 0.15% (w/v)"); and (3) that it was well known in the art how to determine the most efficacious ophthalmically acceptable dose (*e.g.*, 0.15%). Beck was cited for its disclosure of a chlorite preservative component.

57. In the only substantive Office Action during prosecution of the Parent Application (from which the '210 patent matured), mailed on January 15, 2003, the Patent Examiner rejected all pending claims as obvious over Burke in view of Remington's Pharmaceutical Sciences. The wording of the Examiner's rejection with respect to Burke was identical to that in the '834 patent's prosecution except that, rather than noting Burke failed to disclose a chlorite preservative component, the Examiner stated (erroneously) that Burke did not disclose the solubility enhancing agent to be carboxymethylcellulose (hereinafter "CMC") or the pH of its composition. Remington was cited for its disclosure of CMC.

58. On February 25, 2003, Allergan's attorney, Carlos A. Fisher, held a telephonic interview(s) with the Patent Examiner regarding the applications that matured into the '210 and '834 patents. With respect to the pending claims in the Parent Application (which matured into the '210 patent), Allergan "explained the instant invention was an invention of selection" and "agreed to file a declaration showing unexpected results with regards to the anionic solubility enhancing agent [*i.e.*, CMC]." With respect to the pending claims in the application that matured into the '834 patent, Allergan "explained the advantages of the composition comprising up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinozaline tartrate, wherein the composition has a pH of about 7.0 or greater were unexpected" and "agreed to file a declaration showing the unexpected results."

59. In the only Office Action during prosecution of the '337 patent, dated March 3, 2003 and mailed March 13, 2003, the Patent Examiner rejected all pending claims as obvious over Burke in view of Beck. The wording of the Examiner's rejection with respect to Burke was largely identical to that in the applications that matured into the '210 and '834 patents, except that the Examiner stated (correctly) that Burke disclosed CMC. Beck was cited for its disclosure of a chlorite preservative component.

60. On March 12, 2003, Allergan submitted a "Reply to Office Action" in the Parent Application. The Reply, executed by Carlos Fisher, was accompanied by a "Declaration of Orest Olejnik, Ph.D." These documents were received by the Examiner's technology center at the PTO on March 24, 2003.

61. The Reply to Office Action amended the pending claims to require, *inter alia*, that the claimed composition be a "therapeutically effective aqueous composition," comprising a 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, or a salt or ester thereof, in a therapeutically effective amount and a "polyanionic" or "anionic" solubility enhancing component. The

applicants also added several new dependent claims to compositions further comprising oxy-chloro preservative components. None of the claims contained a limitation regarding the adherence or adsorption of the compositions to cell surfaces.

62. The March 12, 2003 Reply argued, in response to the outstanding obviousness rejection, that anionic solubility enhancing components such as CMC have "surprising" properties in the solubilization of brimonidine as compared to non-ionic or cationic polymers, stating, in part, that (p.7):

> In light of Dr. Olejnik's Declaration, the patent specification and the state of the art, the Applicants therefore submit that, alone or in combination with Remington, 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 '991 patent.

63. In the accompanying Declaration of Orest Olejnik, Ph.D., Dr. Orest Olejnik, Allergan's Director of Pharmaceutical Development, stated, in part, that (¶¶6-8):

> Neither Burke nor Remington discloses that CMC would have any characteristics that would motivate a person or ordinary skill in the art to choose it over the other polymers in formulating a brimonidine solution.
>
> Unlike the other listed polymers (polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers, and hydroxyethylcellulose), CMC is anionic at pH7 or greater. The other listed polymers are non-ionic polymers. I have discovered as a result of work done and/or directed by me at Allergan that CMC possesses the surprising advantages of both increasing the solubility in solution, as shown in Table 1, and causing such solutions to have superior adherence to cell surfaces, including ocular surfaces such as the cornea. Polyvinyl alcohol was found not to possess both of these properties. Increased adherence of the CMC solution is particularly surprising given the fact that the corneal surface is negatively charged; one would expect less adherence in such a solution due to electrostatic repulsion, rather than increased adherence. . . .
>
> 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 [sic] in so way would render the presently claimed compositions obvious to the worker of ordinary (or even extraordinary) skill in the art.

64. Five days after mailing the Reply and Declaration in the Parent Application, Allergan mailed a "Reply to Office Action" in the prosecution of the application that matured into the '834 patent on March 17, 2003. The March 17, 2003 Reply, executed by Carlos Fisher, was accompanied by a "Declaration of Amy Batoosingh." These documents were received by the Patent Examiner's technology center on March 28, 2003.

65. The March 17, 2003 Reply amended the pending claims to require, *inter alia*, that the claimed composition be a "therapeutically effective aqueous composition." Allergan also argued, with respect to the outstanding obviousness rejection, in part, that (p. 4-5):

> 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 (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.
>
> * * *
>
> 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 . . . 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.

66. In the accompanying "Declaration of Amy Batoosingh," Amy Batoosingh, Allergan's Director of Ophthalmological Clinical Research, stated, in part, with respect to Katz *et al.*, 2002, *J. Glaucoma* 11:119, that (¶4):

> The conclusion reached as a result of the studies referenced in the Katz et al., article was that brimonidine 0.2% and brimonidine-Purite 0.15% showed comparable efficacy when each was used for treatment of ocular hypertension in glaucoma and/or ocular hypotensive human patients over a 12 month period of time, despite a significant reduction in the concentration of the active ingredient in the latter formulation.

67. On June 3, 2003, the Patent Examiner sent Allergan Notices of Allowance with respect to the claims of the '210 and '834 patents. The '210 and '834 patents issued on September 30, 2003 and November 4, 2003, respectively, without further prosecution.

68. Allergan mailed its Reply to Office Action in the prosecution of the '337 patent on June 13, 2003, ten days after the Patent Examiner issued Notices of Allowance with respect to the '210 and '834 patents. The Reply was executed by Allergan's attorney, Carlos Fisher. Allergan amended the pending claims to require, *inter alia*, that the claimed composition be "therapeutically effective" and contain an SEC other than a cyclodextrin. Allergan did not underline the requirement for "a solubility enhancing component" to indicate that it had been added in the amendment. Allergan also deleted the oxy-chloro limitation, which had been its

purported reason for filing the divisional application. In response to the Examiner's obviousness rejection, Allergan argued, in part, that (p. 5):

> 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 formlated [sic: formulated)], is, to the Applicants' knowledge, the first reference to do so.

69. On October 4, 2003, the Patent Examiner sent Allergan a Notice of Allowance with respect to the '337 patent. The '337 patent issued on January 6, 2004 without further substantive prosecution.

70. At the time of filing, and during the prosecution of '210 patent application, Allergan made misrepresentations and/or omissions of material facts to the Patent Examiner and the United States Patent Office, including, but not limited to, the following:

a. Allergan represented and/or clearly implied that it had conducted comparative experiments with respect to solubility and/or adherence to cell surfaces. That representation and/or implication was false.

b. Allergan represented and/or clearly implied that polyvinyl alcohol, povidone, hydroxypropyl methyl cellulose, poloxamers, and/or hydroxyethyl cellulose were not solubility enhancing agents, not adhesive agents, and/or not solubility enhancing agents and not adhesive agents. The inventor(s), prosecuting attorney(s) and/or others substantively involved in the prosecution of the '210 patent believed that representation and/or implication to be false.

c. Allergan represented and/or clearly implied that CMC had "surprising" properties as a solubility enhancing agent, an adhesive agent, and/or a solubility enhancing and an adhesive agent. That representation and/or implication was false.

d. Allergan represented and/or clearly implied that its alleged invention was patentable as an "invention of selection." That representation and/or implication was false and/or misleading because the invention of selection argument was inapplicable.

e. Allergan represented and/or clearly implied that the other "vehicles" disclosed in Burke did not have solubility enhancing properties, when it believed otherwise.

f. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the best mode contemplated by the inventor(s) of carrying out the invention. Among other things, Allergan had filed a New Drug Application ("NDA") for a commercial product, which reflected the subject matter claimed by the '210 patent, shortly before filing the earliest application giving rise to the '210 patent. Whereas the NDA disclosed, *inter alia*, a "therapeutically effective aqueous composition" with brimonidine "in an amount effective to provide a therapeutic effect" and a polyanionic SEC "in an amount effective to increase the solubility of" the brimonidine, that composition was not disclosed in the '210 patent.

g. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the existence of prior published information contradicting its representations with respect to adhesive properties of the "vehicles" disclosed in Burke, including, but not limited to:

   i. Greaves et al., 1992, *STP Pharma Sci.*, 2:13-33

   ii. J.D. Smart, 1984, *J. Pharmacol.*, 36:295-299

   iii. M.F. Saettone, 1984, *Int'l J. Pharmaceutics*, 20:187-202

h. On information and belief, Allergan suppressed, and failed to disclose to the PTO, information contradicting its representations with respect to the solubilizing properties of the "vehicles" disclosed in Burke.

i. On information and belief, Allergan suppressed, and failed to disclose to the PTO, other information contradicting its representations with respect to adhesive properties of the "vehicles" disclosed in Burke.

71. At the time of filing, and during the prosecution of '834 patent application, Allergan made misrepresentations and/or omissions of material facts to the Patent Examiner and the United States Patent Office, including, but not limited to:

a. Allergan represented and/or clearly implied that it was "surprising" that the concentration of active ingredient in a therapeutically effective composition could be reduced by adjusting the composition's pH closer to the pKa of the active ingredient. That representation and/or implication was false.

b. Allergan represented that it was "truly unexpected" that "a therapeutically effective dosage could be provided by a composition containing about 0.15% or less of brimonidine" at a pH greater than about 7.0. That representation was false.

c. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the best mode contemplated by the inventor(s) (whether named on the '834 patent or not) of carrying out the invention. Among other things, Allergan had filed an NDA for a commercial product, which reflected the subject matter claimed by the '834 patent, shortly before filing the earliest application giving rise to the '834 patent. Whereas the NDA disclosed, *inter alia*, a therapeutically effective aqueous ophthalmic composition with 0.15% brimonidine, that composition was not disclosed in the '834 patent.

d. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the existence of prior published information demonstrating the efficacy of brimonidine at concentrations of "up to about 0.15%," including, but not limited to:

i. Derick et al., 1997, *Ophthalmol.*, 104:131-136

ii. Walters T, 1996, *Survey of Ophthalmol.*, 41:S19-S26

e. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the existence of prior published information demonstrating the effect of pH on drug bioavailability, including, but not limited to:

i. Olejnik, O., 1992, Ophthalmic Drug Delivery Systems (Ashim Mitra, ed.) pp. 177-198.

ii. Wilson et al., 1981, *J. Pharm. Pharmacol.*, 31:749-53.

iii. Small et al., 1997, *Int'l J. Pharmaceutics*, 149: 195-201.

iv. Chien et al., 1990, *Current Eye Res.*, 9:1051-1059.

72. At the time of filing, and during the prosecution of the '337 patent application, Allergan made misrepresentations and/or omissions of material facts to the Patent Examiner and the United States Patent Office, including, but not limited to:

a. Allergan represented that "nothing in Burke discloses or suggests the use of a solubility enhancing component in combination with an alpha adrenergic agonist." Allergan clearly understood that Burke disclosed an alpha adrenergic agonist in combination with a "vehicle," and failed to disclose its belief that nearly all of the "vehicles" disclosed in Burke functioned as solubility enhancing components (albeit not labeled as such).

b. Allergan represented and/or clearly implied that its patent application was, to the Applicants' knowledge, the first reference to disclose the advantages of using a solubility enhancing component, "such as greater flexibility with the concentration and pH at which such composition is formulated." That representation and/or implication was false.

c. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the best mode contemplated by the inventor(s) of carrying out the invention. Among other things, Allergan had filed an NDA for a commercial product, which reflected the subject matter claimed by the '337 patent, shortly before filing the earliest application giving rise to the '337 patent. Whereas the NDA disclosed, *inter alia*, a "therapeutically effective aqueous composition" with brimonidine "in an amount effective to provide a therapeutic effect" and an SEC "in an amount effective to increase the solubility of" the brimonidine, that composition was not disclosed in the '337 patent.

d. On information and belief, Allergan suppressed, and failed to disclose to the PTO prior published information contradicting its representation that, to the Applicants' knowledge, the '337 patent's specification was the first reference to disclose the advantages of using a solubility enhancing component, "such as greater flexibility with the concentration and pH at which such composition is formulated," including, but not limited to, the references identified in paragraphs 70 and 71.

73. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were false and/or misleading.

74. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were material to the prosecution of the '210, '834 and/or '337 patents.

75. The representations and/or omissions set forth in paragraph 70 were material to the prosecution of the '210, '834 and '337 patents.

76. The representations and/or omissions set forth in paragraph 71 were material to the prosecution of the '210, '834 and '337 patents.

77. The representations and/or omissions set forth in paragraph 72 were material to the prosecution of the '337 patent.

78. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were known, or should have been known, by Allergan to be false and/or misleading prior to the issuance of the '210, '834 and/or '337 patents.

79. Allergan knew, or should have known, that the representations and/or omissions set forth in paragraphs 70, 71 and 72 were material to the prosecution of the '210, '834 and/or '337 patents.

80. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were made with the intent to, and/or did, deceive the PTO, and were intended to, and/or did, induce the issuance of the '210, '834 and/or '337 patents.

81. Allergan (including, without limitation, its inventors, attorneys, and/or others involved in the filing and/or prosecution of the '210, '834 and/or '337 patents) owed a duty of candor and good faith to the United States Patent and Trademark Office.

82. The first named inventor of the '210, '834 and '337 patents, Orest Olejnik, owed a duty of candor and good faith to the United States Patent and Trademark Office.

83. An attorney who prosecuted the '210, '834 and '337 patents for Allergan, Carlos A. Fisher, owed a duty of candor and good faith to the United States Patent and Trademark Office.

84. Allergan (including, without limitation, its inventors, attorneys, and/or others involved in the filing and/or prosecution of the '210, '834 and/or '337 patents) breached that duty of candor and good faith.

85. The first named inventor of the '210, '834 and '337 patents, Orest Olejnik, breached his duty of candor and good faith to the United States Patent and Trademark Office.

86. An attorney who prosecuted the '210, '834 and '337 patents for Allergan, Carlos A. Fisher, breached his duty of candor and good faith to the United States Patent and Trademark Office.

First Counterclaim For Declaratory Relief

87. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

88. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claims of the '834 patent, literally or under the doctrine of equivalents.

Second Counterclaim For Declaratory Relief

89. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

90. The '834 patent is invalid for failure to comply with one or more requirements of Title 35, U.S.C. sections 102, 103, 112 and/or 256.

Third Counterclaim For Declaratory Relief

91. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

92. The '834 patent is unenforceable for inequitable conduct and/or unclean hands.

Fourth Counterclaim For Declaratory Relief

93. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

94. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claims of the '337 patent, literally or under the doctrine of equivalents.

Fifth Counterclaim For Declaratory Relief

95. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

96. The '337 patent is invalid for failure to comply with one or more requirements of Title 35, U.S.C. sections 102, 103, and/or 112.

Sixth Counterclaim For Declaratory Relief

97. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

98. The '337 patent is unenforceable for inequitable conduct and/or unclean hands.

Seventh Counterclaim For Declaratory Relief

99. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

100. Allergan is barred from recovery for unclean hands.

DEMAND FOR JUDGMENT

WHEREFORE, Alcon respectfully requests:

A. On the Complaint of Allergan, Inc. and Allergan Sales, LLC. (collectively "Allergan") against Alcon:

1. that judgment be entered against Allergan, and in favor of Alcon;

2. that Allergan not be awarded any of the relief it seeks in this action;

3. that no Order be issued under 35 U.S.C. §271(e)(4)(A) affecting FDA approval of Alcon's NDA No. 21-764;

4. that no injunction be entered against Alcon, its officers, agents, servants or employees;

5. that judgment be entered declaring that Alcon has not infringed, and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,641,834 (the "'834 patent") as the result of the making , using or selling of its proposed brimonidine product;

6. that judgment be entered declaring that Alcon has not infringed, and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,673,337 (the "'337 patent") as the result of the making , using or selling of its proposed brimonidine product;

7. that judgment be entered declaring the '834 patent is invalid;

8. that judgment be entered declaring the '834 patent is unenforceable;

9. that judgment be entered declaring the '337 patent is invalid;

10. that judgment be entered declaring the '337 patent is unenforceable;

11. that judgment be entered declaring Allergan is barred from recovery for unclean hands.

B. On Alcon's First Counterclaim, that judgment be entered declaring that Alcon has not infringed and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,641,834 (the "'834 patent")

C. On Alcon's Second Counterclaim, that judgment be entered declaring that each claim of United States Patent No. 6,641,834 (the "'834 patent") is invalid;

D. On Alcon's Third Counterclaim, that judgment be entered declaring that United States Patent No. 6,641,834 (the "'834 patent") is unenforceable;

E. On Alcon's Fourth Counterclaim, that judgment be entered declaring that Alcon has not infringed and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,673,337 (the "'337 patent");

F. On Alcon's Fifth Counterclaim, that judgment be entered declaring that each claim of United States Patent No. 6,673,337 (the "'337 patent") is invalid;

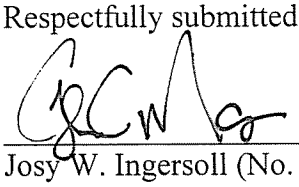
G. On Alcon's Sixth Counterclaim, that judgment be entered declaring that United States Patent No. 6,673,337 (the "'337 patent") is unenforceable;

H. On Alcon's Seventh Counterclaim, that judgment be entered declaring that Allergan is barred from recovery for unclean hands;

I. That this case be declared exceptional and that Alcon be awarded its attorney's fees, costs, and expenses; and

J. That Alcon be awarded such other and further relief as this Court may deem just and proper.

Respectfully submitted,



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July 25, 2005

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

FIRST AMENDED ANSWER AND COUNTERCLAIMS

Defendants, Alcon Inc., Alcon Laboratories, Inc. and Alcon Research Ltd. (collectively "Alcon"), for their Amended Answer to the Complaint filed by Allergan, Inc. and Allergan Sales, LLC. (collectively "Allergan"), state as follows:

The Nature of the Action

1. Alcon admits that paragraph 1 of the Complaint alleges infringement of United States Patents Nos. 6,641,834 ("the '834 patent") and 6,673,337 ("the '337 patent").

The Parties

2. Alcon admits the allegations of paragraph 2 of the Complaint.

3. Alcon admits the allegations of paragraph 3 of the Complaint.

4. Alcon admits the allegations of paragraph 4 of the Complaint.

Jurisdiction and Venue

5. Alcon admits the allegations of paragraph 5 of the Complaint.

6. Alcon admits the allegations of paragraph 6 of the Complaint.

Background

7. Alcon admits that the '834 patent reflects that such patent, entitled "Compositions Containing Alpha-2-Adrenergic Agonist Components," issued to Orest Olejnik and Edward D.S. Kerslake on November 4, 2003, but denies that a true and accurate copy of same is annexed to the Complaint as Exhibit A as alleged in paragraph 7 of the Complaint.

8. Alcon lacks knowledge or information sufficient to form a belief as to the truth of the allegations in paragraph 8 of the Complaint and therefore denies such allegations.

9. Alcon admits that the '337 patent reflects that such patent, entitled "Compositions Containing Alpha-2-Adrenergic Agonist Components," issued to Orest Olejnik and Edward D.S. Kerslake on January 6, 2003, and that a copy of same is annexed to the Complaint as Exhibit B as alleged in paragraph 9 of the Complaint.

10. Alcon lacks knowledge or information sufficient to form a belief as to the truth of the allegations in paragraph 10 of the Complaint and therefore denies such allegations.

11. Alcon admits the allegations of paragraph 11 of the Complaint.

12. Upon information and belief, Alcon admits that ALPHAGAN®P is encompassed within the scope of at least one claim of the '834 patent and at least one claim of the '337 patent.

13. Alcon lacks knowledge or information sufficient to form a belief as to the truth of the allegation that pediatric exclusivity was granted on December 20, 2001, and therefore denies such allegation, but admits the remaining allegations of paragraph 13 of the Complaint.

14. Alcon admits the allegations of paragraph 14 of the Complaint.

15. Alcon admits the allegations of paragraph 15 of the Complaint.

Count I

16. Alcon repeats and realleges the responses to the allegations in paragraphs 1 through 15 hereof as though fully set forth herein.

17. Alcon denies that it has committed an act of infringement under 35 U.S.C. §271(e)(2) by submitting NDA No. 21-764 or otherwise, but admits that Alcon submitted NDA No. 21-764 to the FDA under 505(b)(2) of the FDCA to obtain approval to engage in the commercial manufacture and sale of its proposed Brimonidine Tartrate Ophthalmic Solution 0.15% product.

18. Alcon denies the allegations of paragraph 18 of the Complaint.

19. Alcon denies the allegations of paragraph 19 of the Complaint.

Count II

20. Alcon repeats and realleges the responses to the allegations in paragraphs 1 through 15 hereof as though fully set forth herein.

21. Alcon denies that it has committed an act of infringement under 35 U.S.C. §271(e)(2) by submitting NDA No. 21-764 or otherwise, but admits that Alcon submitted NDA No. 21-764 to the FDA under section 505(b)(2) of the FDCA to obtain approval to engage in the commercial manufacture and sale of its proposed Brimonidine Tartrate Ophthalmic Solution 0.15% product.

22. Alcon denies the allegations of paragraph 22 of the Complaint.

23. Alcon denies the allegations of paragraph 23 of the Complaint.

AFFIRMATIVE DEFENSES

Alcon, for its affirmative defenses to the allegations in Counts I and II of the Complaint, alleges as follows:

First Affirmative Defense

24. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claim of the '834 patent, literally or under the doctrine of equivalents.

Second Affirmative Defense

25. Allergan is estopped from asserting that Alcon will infringe any claims of the '834 patent due to the amendments, arguments and other statements made by or on behalf of applicants during prosecution before the United States Patent and Trademark Office of the applications resulting in issuance of such patent.

Third Affirmative Defense

26. The '834 patent is invalid for failure to comply with one or more requirements of Title 35, United States Code, sections 102, 103, 112, and/or 256.

Fourth Affirmative Defense

27. The '834 patent is unenforceable because, as described in the counterclaims section below, during prosecution of one or more applications related to the '834 patent, person(s) charged with a duty of candor and good faith before the United States Patent and Trademark Office failed to discharge that duty and engaged in inequitable conduct.

Fifth Affirmative Defense

28. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claim of the '337 patent, literally or under the doctrine of equivalents.

Sixth Affirmative Defense

29. Allergan is estopped from asserting that Alcon's proposed brimonidine product will infringe any claims of the '337 patent due to the amendments, arguments and other

statements made by or on behalf of applicants during prosecution before the United States Patent and Trademark Office of the applications resulting in issuance of such patent.

Seventh Affirmative Defense

30. The '337 patent is invalid for failure to comply with one or more requirements of Title 35, United States Code, sections 102, 103 and/or 112.

Eighth Affirmative Defense

31. The '337 patent is unenforceable because, as described in the counterclaims section below, during prosecution of one or more applications related to the '337 patent, person(s) charged with a duty of candor and good faith before the United States Patent and Trademark Office failed to discharge that duty and engaged in inequitable conduct.

Ninth Affirmative Defense

32. Upon information and belief, Allergan is barred from recovery pursuant to the doctrine of unclean hands as described in the counterclaims section below.

COUNTERCLAIMS

Alcon, for its counterclaims herein against Allergan, alleges as follows:

Nature of the Action

33. This is an action for a judgment declaring United States Patent Nos. 6,641,834 (the "'834 patent") and 6,673,337 (the "'337 patent") invalid, not infringed, and unenforceable.

The Parties

34. Alcon Laboratories, Inc. is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 6201 South Freeway, Forth Worth, Texas.

35. Alcon Research, Ltd. is a limited partnership organized and existing under the laws of the state of Texas and has its principal place of business in Fort Worth, Texas.

36. Alcon, Inc. is a corporation organized and existing under the laws of Switzerland and has its principal place of business in Hunenberg, Switzerland.

37. Allergan, Inc. is a corporation organized and existing under the laws of the State of Delaware and has its principal place of business at 2525 Dupont Drive, Irvine, California.

38. Allergan Sales, LLC. is a limited liability company organized and existing under the laws of the State of Delaware and has its principal place of business at 2525 Dupont Drive, Irvine, California.

Jurisdiction and Venue

39. This court has subject matter jurisdiction over this action under the Declaratory Judgment Act and the Patent Laws of the United States, more particularly under Title 28, U.S.C. sections 2201 and 2202 and Title 35, U.S.C. section 1 *et seq.* An actual case or controversy exists between Alcon and Allergan as to the validity, infringement, and enforceability of the '834 and '337 patents, as evidenced by the Complaint and Answer in this action.

40. Venue is proper in this Court pursuant to Title 28, U.S.C. sections 1391(b) and (c).

Factual Background

41. The patents most relevant to this suit include:

a. U.S. Patent No. 6,627,210 (hereinafter "the '210 patent"), which issued on or about September 30, 2003. The '210 patent claims, *inter alia*, a therapeutically effective aqueous composition comprising a 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, or a salt or ester thereof, in a therapeutically effective amount and a polyanionic solubility enhancing component.

b. U.S. Patent No. 6,641,834 (hereinafter "the '834 patent"), which issued on or about November 4, 2003. The '834 patent claims, *inter alia*, a therapeutically effective aqueous ophthalmic composition having a pH of about 7.0 or greater comprising up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline tartrate being soluble in the composition at about 21°C.

c. U.S. Patent No. 6,673,337 (hereinafter "the '337 patent"), which issued on or about January 6, 2004. The '337 patent claims, *inter alia*, a therapeutically effective ophthalmic composition comprising an alpha-2-adrenergic agonist component other than a cyclodextrin in a therapeutically effective amount and a solubility enhancing component.

42. The '834 and '337 patents both claim benefit to Application Serial No. 09/904,018 ("the Parent Application"), which matured into the '210 patent. The '834 patent matured from a continuation application of the Parent Application. The '337 patent matured from a divisional application of the Parent Application.

43. The '210, '834 and '337 patents contain the same specification (but for, understandably, differences in the claims and the section entitled "Cross Reference to Related Application").

44. The '210, '834 and '337 patents each claim therapeutically effective compositions.

45. The '210, '834 and '337 patents each name Orest Olejnik and Edward D.S. Kerslake as their inventors, who are, and/or were, employed by Allergan.

46. The '210, '834 and '337 patents were each prosecuted by, or on behalf of, Allergan.

47. The '210, '834 and '337 patents were each examined by Rachel M. Bennett (hereinafter "Patent Examiner") for the United States Patent and Trademark Office (hereinafter "PTO").

48. During prosecution of the applications that matured into '210, '834 and '337 patents, each claim of each application was rejected as obvious under 35 U.S.C. § 103 over, *inter alia*, the prior art Burke reference (United States Patent No. 5,215,991) and subsequently amended prior to issuance.

49. Carlos A. Fisher, then an Allergan employee, was an attorney of record in connection with the prosecution of the applications that matured into the '210, '834 and '337 patents on behalf of Allergan after the claims in those applications were rejected over Burke.

50. Allergan has alleged that Alcon infringes the '834 and '337 patents.

51. Allergan does not allege that Alcon infringes the '210 patent.

Allergan's Procurement of the '210, '834 and '337 Patents By Inequitable Conduct

52. The subject matter and prosecution of the '210, '834 and '337 patents are intertwined.

53. Allergan filed the Parent Application, which matured into the '210 patent, on July 21, 2001. That application, naming Orest Olejnik as the first inventor, claimed, *inter alia*, a composition comprising an alpha-2-adrenergic agonist in a therapeutically effective amount and a solubility enhancing component.

54. The application that matured into the '834 patent was filed on September 6, 2002. That application was accompanied by a Preliminary Amendment that cancelled all pending claims and added claims to a composition containing, *inter alia*, "up to about 0.15% (w/v)" of brimonidine tartrate.

55. The application that matured into the '337 patent was filed on November 19, 2002, as a divisional application of the Parent Application, and was directed to compositions containing an oxy-chloro preservative. The application was accompanied by a Preliminary Amendment that cancelled all pending claims and added claims to a composition containing, *inter alia*, an alpha-2-adrenergic agonist in a therapeutically effective amount and an oxy-chloro preservative component.

56. In the only Office Action during prosecution of the '834 patent, mailed on December 18, 2002, the Examiner rejected all pending claims as obvious over the Burke (U.S. Patent No. 5,215,991) in view of Beck et al. (U.S. Patent No. 6358935). The Patent Examiner noted that Burke disclosed: (1) the claimed compound, 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, among its most preferred alpha-2-adrenergic compounds; (2) at a concentration from about 0.001% to about 1.0% (w/v), which encompassed the concentration range in the claims ("up to about 0.15% (w/v)"); and (3) that it was well known in the art how to determine the most efficacious ophthalmically acceptable dose (*e.g.*, 0.15%). Beck was cited for its disclosure of a chlorite preservative component.

57. In the only substantive Office Action during prosecution of the Parent Application (from which the '210 patent matured), mailed on January 15, 2003, the Patent Examiner rejected all pending claims as obvious over Burke in view of Remington's Pharmaceutical Sciences. The wording of the Examiner's rejection with respect to Burke was identical to that in the '834 patent's prosecution except that, rather than noting Burke failed to disclose a chlorite preservative component, the Examiner stated (erroneously) that Burke did not disclose the solubility enhancing agent to be carboxymethylcellulose (hereinafter "CMC") or the pH of its composition. Remington was cited for its disclosure of CMC.

58. On February 25, 2003, Allergan's attorney, Carlos A. Fisher, held a telephonic interview(s) with the Patent Examiner regarding the applications that matured into the '210 and '834 patents. With respect to the pending claims in the Parent Application (which matured into the '210 patent), Allergan "explained the instant invention was an invention of selection" and "agreed to file a declaration showing unexpected results with regards to the anionic solubility enhancing agent [*i.e.*, CMC]." With respect to the pending claims in the application that matured into the '834 patent, Allergan "explained the advantages of the composition comprising up to about 0.15% (w/v) of 5-bromo-6-(2-imidozolin-2-ylamino) quinozaline tartrate, wherein the composition has a pH of about 7.0 or greater were unexpected" and "agreed to file a declaration showing the unexpected results."

59. In the only Office Action during prosecution of the '337 patent, dated March 3, 2003 and mailed March 13, 2003, the Patent Examiner rejected all pending claims as obvious over Burke in view of Beck. The wording of the Examiner's rejection with respect to Burke was largely identical to that in the applications that matured into the '210 and '834 patents, except that the Examiner stated (correctly) that Burke disclosed CMC. Beck was cited for its disclosure of a chlorite preservative component.

60. On March 12, 2003, Allergan submitted a "Reply to Office Action" in the Parent Application. The Reply, executed by Carlos Fisher, was accompanied by a "Declaration of Orest Olejnik, Ph.D." These documents were received by the Examiner's technology center at the PTO on March 24, 2003.

61. The Reply to Office Action amended the pending claims to require, *inter alia*, that the claimed composition be a "therapeutically effective aqueous composition," comprising a 5-bromo-6-(2-imidozolin-2-ylamino) quinoxaline, or a salt or ester thereof, in a therapeutically effective amount and a "polyanionic" or "anionic" solubility enhancing component. The

applicants also added several new dependent claims to compositions further comprising oxy-chloro preservative components. None of the claims contained a limitation regarding the adherence or adsorption of the compositions to cell surfaces.

62. The March 12, 2003 Reply argued, in response to the outstanding obviousness rejection, that anionic solubility enhancing components such as CMC have "surprising" properties in the solubilization of brimonidine as compared to non-ionic or cationic polymers, stating, in part, that (p.7):

> In light of Dr. Olejnik's Declaration, the patent specification and the state of the art, the Applicants therefore submit that, alone or in combination with Remington, 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 '991 patent.

63. In the accompanying Declaration of Orest Olejnik, Ph.D., Dr. Orest Olejnik, Allergan's Director of Pharmaceutical Development, stated, in part, that (¶¶6-8):

> Neither Burke nor Remington discloses that CMC would have any characteristics that would motivate a person or ordinary skill in the art to choose it over the other polymers in formulating a brimonidine solution.
>
> Unlike the other listed polymers (polyvinyl alcohol, povidone (polyvinylpyrrolidone), hydroxypropylcellulose, poloxamers, and hydroxyethylcellulose), CMC is anionic at pH7 or greater. The other listed polymers are non-ionic polymers. I have discovered as a result of work done and/or directed by me at Allergan that CMC possesses the surprising advantages of both increasing the solubility in solution, as shown in Table 1, and causing such solutions to have superior adherence to cell surfaces, including ocular surfaces such as the cornea. Polyvinyl alcohol was found not to possess both of these properties. Increased adherence of the CMC solution is particularly surprising given the fact that the corneal surface is negatively charged; one would expect less adherence in such a solution due to electrostatic repulsion, rather than increased adherence. . . .
>
> 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 [sic] in so way would render the presently claimed compositions obvious to the worker of ordinary (or even extraordinary) skill in the art.

64. Five days after mailing the Reply and Declaration in the Parent Application, Allergan mailed a "Reply to Office Action" in the prosecution of the application that matured into the '834 patent on March 17, 2003. The March 17, 2003 Reply, executed by Carlos Fisher, was accompanied by a "Declaration of Amy Batoosingh." These documents were received by the Patent Examiner's technology center on March 28, 2003.

65. The March 17, 2003 Reply amended the pending claims to require, *inter alia*, that the claimed composition be a "therapeutically effective aqueous composition." Allergan also argued, with respect to the outstanding obviousness rejection, in part, that (p. 4-5):

> 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 (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.
>
> * * *
>
> 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 . . . 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.

66. In the accompanying "Declaration of Amy Batoosingh," Amy Batoosingh, Allergan's Director of Ophthalmological Clinical Research, stated, in part, with respect to Katz *et al.*, 2002, *J. Glaucoma* 11:119, that (¶4):

> The conclusion reached as a result of the studies referenced in the Katz et al., article was that brimonidine 0.2% and brimonidine-Purite 0.15% showed comparable efficacy when each was used for treatment of ocular hypertension in glaucoma and/or ocular hypotensive human patients over a 12 month period of time, despite a significant reduction in the concentration of the active ingredient in the latter formulation.

67. On June 3, 2003, the Patent Examiner sent Allergan Notices of Allowance with respect to the claims of the '210 and '834 patents. The '210 and '834 patents issued on September 30, 2003 and November 4, 2003, respectively, without further prosecution.

68. Allergan mailed its Reply to Office Action in the prosecution of the '337 patent on June 13, 2003, ten days after the Patent Examiner issued Notices of Allowance with respect to the '210 and '834 patents. The Reply was executed by Allergan's attorney, Carlos Fisher. Allergan amended the pending claims to require, *inter alia*, that the claimed composition be "therapeutically effective" and contain an SEC other than a cyclodextrin. Allergan did not underline the requirement for "a solubility enhancing component" to indicate that it had been added in the amendment. Allergan also deleted the oxy-chloro limitation, which had been its

purported reason for filing the divisional application. In response to the Examiner's obviousness rejection, Allergan argued, in part, that (p. 5):

> 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 formlated [sic: formulated)], is, to the Applicants' knowledge, the first reference to do so.

69. On October 4, 2003, the Patent Examiner sent Allergan a Notice of Allowance with respect to the '337 patent. The '337 patent issued on January 6, 2004 without further substantive prosecution.

70. At the time of filing, and during the prosecution of '210 patent application, Allergan made misrepresentations and/or omissions of material facts to the Patent Examiner and the United States Patent Office, including, but not limited to, the following:

a. Allergan represented and/or clearly implied that it had conducted comparative experiments with respect to solubility and/or adherence to cell surfaces. That representation and/or implication was false.

b. Allergan represented and/or clearly implied that polyvinyl alcohol, povidone, hydroxypropyl methyl cellulose, poloxamers, and/or hydroxyethyl cellulose were not solubility enhancing agents, not adhesive agents, and/or not solubility enhancing agents and not adhesive agents. The inventor(s), prosecuting attorney(s) and/or others substantively involved in the prosecution of the '210 patent believed that representation and/or implication to be false.

c. Allergan represented and/or clearly implied that CMC had "surprising" properties as a solubility enhancing agent, an adhesive agent, and/or a solubility enhancing and an adhesive agent. That representation and/or implication was false.

d. Allergan represented and/or clearly implied that its alleged invention was patentable as an "invention of selection." That representation and/or implication was false and/or misleading because the invention of selection argument was inapplicable.

e. Allergan represented and/or clearly implied that the other "vehicles" disclosed in Burke did not have solubility enhancing properties, when it believed otherwise.

f. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the best mode contemplated by the inventor(s) of carrying out the invention. Among other things, Allergan had filed a New Drug Application ("NDA") for a commercial product, which reflected the subject matter claimed by the '210 patent, shortly before filing the earliest application giving rise to the '210 patent. Whereas the NDA disclosed, *inter alia*, a "therapeutically effective aqueous composition" with brimonidine "in an amount effective to provide a therapeutic effect" and a polyanionic SEC "in an amount effective to increase the solubility of" the brimonidine, that composition was not disclosed in the '210 patent.

g. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the existence of prior published information contradicting its representations with respect to adhesive properties of the "vehicles" disclosed in Burke, including, but not limited to:

   i. Greaves et al., 1992, *STP Pharma Sci.*, 2:13-33

   ii. J.D. Smart, 1984, *J. Pharmacol.*, 36:295-299

   iii. M.F. Saettone, 1984, *Int'l J. Pharmaceutics*, 20:187-202

h. On information and belief, Allergan suppressed, and failed to disclose to the PTO, information contradicting its representations with respect to the solubilizing properties of the "vehicles" disclosed in Burke.

i. On information and belief, Allergan suppressed, and failed to disclose to the PTO, other information contradicting its representations with respect to adhesive properties of the "vehicles" disclosed in Burke.

71. At the time of filing, and during the prosecution of '834 patent application, Allergan made misrepresentations and/or omissions of material facts to the Patent Examiner and the United States Patent Office, including, but not limited to:

a. Allergan represented and/or clearly implied that it was "surprising" that the concentration of active ingredient in a therapeutically effective composition could be reduced by adjusting the composition's pH closer to the pKa of the active ingredient. That representation and/or implication was false.

b. Allergan represented that it was "truly unexpected" that "a therapeutically effective dosage could be provided by a composition containing about 0.15% or less of brimonidine" at a pH greater than about 7.0. That representation was false.

c. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the best mode contemplated by the inventor(s) (whether named on the '834 patent or not) of carrying out the invention. Among other things, Allergan had filed an NDA for a commercial product, which reflected the subject matter claimed by the '834 patent, shortly before filing the earliest application giving rise to the '834 patent. Whereas the NDA disclosed, *inter alia*, a therapeutically effective aqueous ophthalmic composition with 0.15% brimonidine, that composition was not disclosed in the '834 patent.

d. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the existence of prior published information demonstrating the efficacy of brimonidine at concentrations of "up to about 0.15%," including, but not limited to:

i. Derick et al., 1997, *Ophthalmol.*, 104:131-136

ii. Walters T, 1996, *Survey of Ophthalmol.*, 41:S19-S26

e. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the existence of prior published information demonstrating the effect of pH on drug bioavailability, including, but not limited to:

i. Olejnik, O., 1992, Ophthalmic Drug Delivery Systems (Ashim Mitra, ed.) pp. 177-198.

ii. Wilson et al., 1981, *J. Pharm. Pharmacol.*, 31:749-53.

iii. Small et al., 1997, *Int'l J. Pharmaceutics*, 149: 195-201.

iv. Chien et al., 1990, *Current Eye Res.*, 9:1051-1059.

72. At the time of filing, and during the prosecution of the '337 patent application, Allergan made misrepresentations and/or omissions of material facts to the Patent Examiner and the United States Patent Office, including, but not limited to:

a. Allergan represented that "nothing in Burke discloses or suggests the use of a solubility enhancing component in combination with an alpha adrenergic agonist." Allergan clearly understood that Burke disclosed an alpha adrenergic agonist in combination with a "vehicle," and failed to disclose its belief that nearly all of the "vehicles" disclosed in Burke functioned as solubility enhancing components (albeit not labeled as such).

b. Allergan represented and/or clearly implied that its patent application was, to the Applicants' knowledge, the first reference to disclose the advantages of using a solubility enhancing component, "such as greater flexibility with the concentration and pH at which such composition is formulated." That representation and/or implication was false.

c. On information and belief, Allergan suppressed, and failed to disclose to the PTO, the best mode contemplated by the inventor(s) of carrying out the invention. Among other things, Allergan had filed an NDA for a commercial product, which reflected the subject matter claimed by the '337 patent, shortly before filing the earliest application giving rise to the '337 patent. Whereas the NDA disclosed, *inter alia*, a "therapeutically effective aqueous composition" with brimonidine "in an amount effective to provide a therapeutic effect" and an SEC "in an amount effective to increase the solubility of" the brimonidine, that composition was not disclosed in the '337 patent.

d. On information and belief, Allergan suppressed, and failed to disclose to the PTO prior published information contradicting its representation that, to the Applicants' knowledge, the '337 patent's specification was the first reference to disclose the advantages of using a solubility enhancing component, "such as greater flexibility with the concentration and pH at which such composition is formulated," including, but not limited to, the references identified in paragraphs 70 and 71.

73. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were false and/or misleading.

74. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were material to the prosecution of the '210, '834 and/or '337 patents.

75. The representations and/or omissions set forth in paragraph 70 were material to the prosecution of the '210, '834 and '337 patents.

76. The representations and/or omissions set forth in paragraph 71 were material to the prosecution of the '210, '834 and '337 patents.

77. The representations and/or omissions set forth in paragraph 72 were material to the prosecution of the '337 patent.

78. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were known, or should have been known, by Allergan to be false and/or misleading prior to the issuance of the '210, '834 and/or '337 patents.

79. Allergan knew, or should have known, that the representations and/or omissions set forth in paragraphs 70, 71 and 72 were material to the prosecution of the '210, '834 and/or '337 patents.

80. The representations and/or omissions set forth in paragraphs 70, 71 and 72 were made with the intent to, and/or did, deceive the PTO, and were intended to, and/or did, induce the issuance of the '210, '834 and/or '337 patents.

81. Allergan (including, without limitation, its inventors, attorneys, and/or others involved in the filing and/or prosecution of the '210, '834 and/or '337 patents) owed a duty of candor and good faith to the United States Patent and Trademark Office.

82. The first named inventor of the '210, '834 and '337 patents, Orest Olejnik, owed a duty of candor and good faith to the United States Patent and Trademark Office.

83. An attorney who prosecuted the '210, '834 and '337 patents for Allergan, Carlos A. Fisher, owed a duty of candor and good faith to the United States Patent and Trademark Office.

84. Allergan (including, without limitation, its inventors, attorneys, and/or others involved in the filing and/or prosecution of the '210, '834 and/or '337 patents) breached that duty of candor and good faith.

85. The first named inventor of the '210, '834 and '337 patents, Orest Olejnik, breached his duty of candor and good faith to the United States Patent and Trademark Office.

86. An attorney who prosecuted the '210, '834 and '337 patents for Allergan, Carlos A. Fisher, breached his duty of candor and good faith to the United States Patent and Trademark Office.

First Counterclaim For Declaratory Relief

87. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

88. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claims of the '834 patent, literally or under the doctrine of equivalents.

Second Counterclaim For Declaratory Relief

89. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

90. The '834 patent is invalid for failure to comply with one or more requirements of Title 35, U.S.C. sections 102, 103, 112 and/or 256.

Third Counterclaim For Declaratory Relief

91. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

92. The '834 patent is unenforceable for inequitable conduct and/or unclean hands.

Fourth Counterclaim For Declaratory Relief

93. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

94. Alcon's proposed brimonidine product will not infringe, contribute to, or induce infringement of any claims of the '337 patent, literally or under the doctrine of equivalents.

Fifth Counterclaim For Declaratory Relief

95. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

96. The '337 patent is invalid for failure to comply with one or more requirements of Title 35, U.S.C. sections 102, 103, and/or 112.

Sixth Counterclaim For Declaratory Relief

97. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

98. The '337 patent is unenforceable for inequitable conduct and/or unclean hands.

Seventh Counterclaim For Declaratory Relief

99. Alcon repeats and realleges the allegations of paragraphs 33 through 86 hereof as though fully set forth herein.

100. Allergan is barred from recovery for unclean hands.

DEMAND FOR JUDGMENT

WHEREFORE, Alcon respectfully requests:

A. On the Complaint of Allergan, Inc. and Allergan Sales, LLC. (collectively "Allergan") against Alcon:

1. that judgment be entered against Allergan, and in favor of Alcon;

2. that Allergan not be awarded any of the relief it seeks in this action;

3. that no Order be issued under 35 U.S.C. §271(e)(4)(A) affecting FDA approval of Alcon's NDA No. 21-764;

4. that no injunction be entered against Alcon, its officers, agents, servants or employees;

5. that judgment be entered declaring that Alcon has not infringed, and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,641,834 (the "'834 patent") as the result of the making , using or selling of its proposed brimonidine product;

6. that judgment be entered declaring that Alcon has not infringed, and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,673,337 (the "'337 patent") as the result of the making , using or selling of its proposed brimonidine product;

7. that judgment be entered declaring the '834 patent is invalid;

8. that judgment be entered declaring the '834 patent is unenforceable;

9. that judgment be entered declaring the '337 patent is invalid;

10. that judgment be entered declaring the '337 patent is unenforceable;

11. that judgment be entered declaring Allergan is barred from recovery for unclean hands.

B. On Alcon's First Counterclaim, that judgment be entered declaring that Alcon has not infringed and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,641,834 (the "'834 patent")

C. On Alcon's Second Counterclaim, that judgment be entered declaring that each claim of United States Patent No. 6,641,834 (the "'834 patent") is invalid;

D. On Alcon's Third Counterclaim, that judgment be entered declaring that United States Patent No. 6,641,834 (the "'834 patent") is unenforceable;

E. On Alcon's Fourth Counterclaim, that judgment be entered declaring that Alcon has not infringed and will not infringe, and is not and will not be liable for any infringement of, any claim of United States Patent No. 6,673,337 (the "'337 patent");

F. On Alcon's Fifth Counterclaim, that judgment be entered declaring that each claim of United States Patent No. 6,673,337 (the "'337 patent") is invalid;

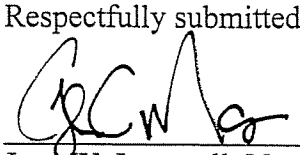
G. On Alcon's Sixth Counterclaim, that judgment be entered declaring that United States Patent No. 6,673,337 (the "'337 patent") is unenforceable;

H. On Alcon's Seventh Counterclaim, that judgment be entered declaring that Allergan is barred from recovery for unclean hands;

I. That this case be declared exceptional and that Alcon be awarded its attorney's fees, costs, and expenses; and

J. That Alcon be awarded such other and further relief as this Court may deem just and proper.

Respectfully submitted,



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