CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-598

ADMINISTRATIVE DOCUMENTS AND CORRESPONDENCE

EXCLUSIVITY SUMMARY for NDA # 21-598

Trade Name Vigamox
Generic Name moxifloxacin HCl ophthalmic solution, 0.5%
Applicant Name Alcon, Inc. HFD-550
Approval Date _____

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

   a) Is it an original NDA? YES/_X_/ NO /___/

   b) Is it an effectiveness supplement? YES /___/ NO /_X_/

   c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

   YES / X / NO /___/

   If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

   _____

   If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

   _____

   _____

   d) Did the applicant request exclusivity?

   YES /_X_/ NO /___/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

3 years

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /_X__/ NO /___/

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC) Switches should be answered No - Please indicate as such).

YES /__/ NO /_X_/

If yes, NDA # _____ Drug Name _____

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

3. Is this drug product or indication a DESI upgrade?

YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES /_X__/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 21-085 _____

NDA # 21-277 _____

NDA # 21-334 _____

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /___/ NO /___/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # _____ _____

NDA # _____ _____

NDA # _____ _____

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

PART III: <u>THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS</u>

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /_X__/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis

for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES /_X__/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

_____

_____

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES /___/ NO /_X_/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES /___/ NO /___/

If yes, explain: _____

_____

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness

of this drug product?

YES /___/ NO /_X_/

If yes, explain: _____

_____

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # C-00-46

Investigation #2, Study # C-00-55

Investigation #3, Study # C-01-34

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /_X_/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # _____ **Study #** _____
NDA # _____ **Study #** _____
NDA # _____ **Study #** _____

(b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /_X_/

Investigation #2 YES /___/ NO /_X_/

Investigation #3 YES /___/ NO /_X_/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # _____ Study # _____

NDA # _____ Study # _____

NDA # _____ Study # _____

(c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation # 1 , Study # C-00-46

Investigation # 2 , Study # C-00-55

Investigation # 3 , Study # C-01-34

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1

IND # ___ YES /_X_/ NO /___/ Explain: _____

_____

Investigation #2

IND # ___ YES /_X_/ NO /___/ Explain: _____

_____

Investigation #3

IND# ___ YES / X /

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____
Investigation #2	
YES /___/ Explain _____	NO /___/ Explain _____
_____	_____
_____	_____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /_X_/

If yes, explain: _____

_____

_____

_____ _____

Signature of Preparer Date

Title: _____

/S/ 4/12/03

Signature of ~~Office of~~ Division Director Date

Deputy

Form OGD-011347
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

PEDIATRIC EXCLUSIVITY DETERMINATION CHECKLIST

PART I - TO BE COMPLETED BY THE REVIEWING DIVISION.

Date of Written Request from FDA 6/26/00. Application Written Request was made to: IND# ___
Timeframe Noted in Written Request for Submission of Studies 1/1/03.
NDA# 21-598 Supplement #_____ Choose one: SE1 SE2 SE3 SE4 SE5 SE6 SE7 SE8 SLR
Sponsor Alcon, Inc.
Generic Name Moxifloxacin Ophthalmic Solution Trade Name undetermined
Strength 0.5% Dosage Form/Route ophthalmic solution
Date of Submission of Reports of Studies 10/14/02.
Pediatric Exclusivity Determination Due Date (90 days from date of submission of studies) ~~1/13/03~~. 1/12/03

Was a formal Written Request made for the pediatric studies submitted?	Y X	N ___
Were the studies submitted after the Written Request?	Y X	N ___
Were the reports submitted as a supplement, amendment to an NDA, or NDA?	Y X	N ___
Was the timeframe noted in the Written Request for submission of studies met?	Y X	N ___
If there was a written agreement, were the studies conducted according to the written agreement? OR If there was no written agreement, were the studies conducted in accord with good scientific principles?	Y X	N ___
Did the studies fairly respond to the Written Request?	Y X	N ___

SIGNED /S/ DATE 1/10/03
(Reviewing Medical Officer)

Do not enter in DFS - FORWARD TO PEDIATRIC EXCLUSIVITY BOARD, HFD-960.

PART II - TO BE COMPLETED BY THE PEDIATRIC EXCLUSIVITY BOARD

Pediatric Exclusivity ✓ **Granted** ___ **Denied**

Existing Patent or Exclusivity Protection:

NDA/Product #	Eligible Patents/Exclusivity	Current Expiration Date
NO UNEXPIRED	PATENTS/EXCLUSIVITIES	AT THIS TIME
APPLICATION	PENDING APPROVAL	

SIGNED /S/ DATE 1/10/03

Revised: 11/30/2001

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Grace Carmouze
1/10/03 05:53:05 PM

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA # : 21-598 Supplement Type (e.g. SE5): N/A Supplement Number: N/A

Stamp Date: October 15, 2002 Action Date: _____

HFD-550 Trade and generic names/dosage form: Vigamox (moxifloxacin HCl ophthalmic solution) 0.5%

Applicant: Alcon, Inc. Therapeutic Class: 3-s

Indication(s) previously approved: N/A

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: treatment of bacterial convunctivitis

Is there a full waiver for this indication (check one)?

☐ Yes: Please proceed to Section A.

X No: Please check all that apply: ____Partial Waiver ____Deferred X Completed
NOTE: More than one may apply
Please proceed to Section B, Section C, and/or Section D and complete as necessary.

ction A: Fully Waived Studies

Reason(s) for full waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population
☐ Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
☐ Other: _____

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section B: Partially Waived Studies

Age/weight range being partially waived:

Min_____	kg_____	mo._____	yr._____	Tanner Stage_____
Max_____	kg_____	mo._____	yr._____	Tanner Stage_____

Reason(s) for partial waiver:

☐ Products in this class for this indication have been studied/labeled for pediatric population
☐ Disease/condition does not exist in children
☐ Too few children with disease to study
☐ There are safety concerns
☐ Adult studies ready for approval
☐ Formulation needed
☐ Other: _____

tudies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

Section C: Deferred Studies

Age/weight range being deferred:

Min _____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**_____	**Tanner Stage**_____

Reason(s) for deferral:

- ☐ **Products in this class for this indication have been studied/labeled for pediatric population**
- ☐ **Disease/condition does not exist in children**
- ☐ **Too few children with disease to study**
- ☐ **There are safety concerns**
- ☐ **Adult studies ready for approval**
- ☐ **Formulation needed**

Other:_____

Date studies are due (mm/dd/yy): _____

If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.

:tion D: Completed Studies

Age/weight range of completed studies:

Min _____	**kg**_____	**mo.**__0__	**yr.**_____	**Tanner Stage**_____
Max_____	**kg**_____	**mo.**_____	**yr.**__18__	**Tanner Stage**_____

Comments:

If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.

This page was completed by:

{See appended electronic signature page}

_____

Regulatory Project Manager

cc: NDA
HFD-950/ Terrie Crescenzi
HFD-960/ Grace Carmouze
(revised 9-24-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960
301-594-7337

NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 21-598	Efficacy Supplement Type N/A	Supplement Number N/A	
Drug: **Vigamox (moxifloxacin HCl ophthalmic solution), 0.5%**		Applicant: **Alcon, Inc.**	
RPM: **Michael Puglisi**		**HFD-550**	Phone # **72522**
Application Type: (X) 505(b)(1) ( ) 505(b)(2)		Reference Listed Drug (NDA #, Drug name):	

❖ Application Classifications:	
• Review priority	(X) Standard ( ) Priority
• Chem class (NDAs only)	3-S
• Other (e.g., orphan, OTC)	
❖ User Fee Goal Dates	**April 15, 2003**
❖ Special programs (indicate all that apply)	(X) None Subpart H ( ) 21 CFR 314.510 (accelerated approval) ( ) 21 CFR 314.520 (restricted distribution) ( ) Fast Track ( ) Rolling Review
❖ User Fee Information	
• User Fee	(X) Paid
• User Fee waiver	( ) Small business ( ) Public health ( ) Barrier-to-Innovation ( ) Other
• User Fee exception	( ) Orphan designation ( ) No-fee 505(b)(2) ( ) Other
❖ Application Integrity Policy (AIP)	
• Applicant is on the AIP	( ) Yes (X) No
• This application is on the AIP	( ) Yes (X No
• Exception for review (Center Director's memo)	N/A
• OC clearance for approval	N/A
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.	(X) Verified
❖ Patent	
• Information: Verify that patent information was submitted	(X) Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted	21 CFR 314.50(i)(1)(*i*)(A) ( ) I ( ) II ( ) III ( ) IV 21 CFR 314.50(i)(1) ( ) (ii) ( ) (iii)
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).	( ) Verified
❖ Exclusivity Summary (approvals only)	X

❖ Administrative Reviews (Project Manager, ADRA) *(indicate date of each review)*	N/A
[redacted]	
❖ Actions	
• Proposed action	(X) AP ( ) TA ( ) AE ( ) NA
• Previous actions (specify type and date for each action taken)	none
• Status of advertising (approvals only)	(X) Materials requested in AP letter ( ) Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	(X) Yes ( ) Not applicable
• Indicate what types (if any) of information dissemination are anticipated	(X) None ( ) Press Release ( ) Talk Paper ( ) Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable)	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	
• Most recent applicant-proposed labeling	April 15, 2003
• Original applicant-proposed labeling	October 14, 2002
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings *(indicate dates of reviews and meetings)*	November 25, 2002 March 21, 2003
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	
• Applicant proposed	April 11, 2003
• Reviews	April 15, 2003
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	N/A
• Documentation of discussions and/or agreements relating to post-marketing commitments	N/A
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	May 7, 2001
• Pre-NDA meeting (indicate date)	N/A
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	1/10/03 Peds Excl. Board Mtg.
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) *(indicate date for each review)*	**N/A**
❖ Clinical review(s) *(indicate date for each review)*	**4/15/03 (two)**
❖ Microbiology (efficacy) review(s) *(indicate date for each review)*	**2/28/03**
❖ Safety Update review(s) *(indicate date or location if incorporated in another review)*	**4/12/03**
❖ Pediatric Page(separate page for each indication addressing status of all age groups)	**X**
❖ Statistical review(s) *(indicate date for each review)* **within clinical review**	**4/15/03**
❖ Biopharmaceutical review(s) *(indicate date for each review)*	**4/7/03**
❖ Controlled Substance Staff review(s) and recommendation for scheduling *(indicate date for each review)*	**N/A**
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	**3/10/03**
• Bioequivalence studies	**N/A**
CMC Information	
❖ CMC review(s) *(indicate date for each review)*	**4/2/03**
❖ Environmental Assessment	
• Categorical Exclusion *(indicate review date)*	**4/2/03**
• Review & FONSI *(indicate date of review)*	**N/A**
• Review & Environmental Impact Statement *(indicate date of each review)*	**N/A**
Micro (validation of sterilization & product sterility) review(s) *(indicate date for each review)*	**3/21/03**
❖ Facilities inspection (provide EER report) **See CMC Review**	Date completed: ( ) Acceptable ( ) Withhold recommendation
❖ Methods validation	( ) Completed (X) Requested ( ) Not yet requested
Nonclinical Pharm/Tox Information	
❖ Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	**2/11/03**
❖ Nonclinical inspection review summary	**N/A**
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	**N/A**
❖ CAC/ECAC report	

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Angela Kothe, Ph.D.	**From:** Mike Puglisi
Fax: 817-551-4630	**Fax:** 301-827-2531
Phone:	**Phone:** 301-827-2522
Pages: 1 (incl. cover)	**Date:** April 2, 2003
Re: BioPharm Comments for ——— (& 21-598)	

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

• **Comments:**

Angela-
Here are some comments from our BioPharm reviewer concerning the moxifloxacin NDA. Please let me know if you have any questions about these comments. Thanks.
–Mike

Comments to the Sponsor:

1. ***While not an impediment to approval, the agency is still awaiting the updated information regarding long-term frozen storage stability of moxifloxacin in human plasma to cover the time period between initiation of these studies and completion of sample analysis.***
2. ***The agency does not agree with the approach to replace below the LOQ (BLQ) values with one half of the LOQ for calculating the mean values for data analysis. In the future, please replace BLQ levels with zero and calculate both mean of all data and mean of measurable values.***

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

INT

Alcon Universal, Ltd.
c/o Alcon Laboratories, Inc.
Attention: Scott Krueger
Senior Director, Regulatory Affairs
6201 South Freeway
Fort Worth, TX 76134-2099

JUN 26 2000

Dear Mr. Krueger:

To obtain needed pediatric information on moxifloxacin hydrochloride for the treatment of bacterial conjunctivitis, the Food and Drug Administration (FDA) is hereby making a formal Written Request, pursuant to Section 505A of the Federal Food, Drug, and Cosmetic Act, that information be submitted from the following study:

Type of Study:
The study should be a randomized, double-masked, parallel comparison trial. The study should be of at least 1 week duration and should include a minimum of three evaluations, for example, baseline, day 3±1 day, and end of treatment.

Indication/Objective:
The primary objective of the study should be to evaluate the safety and efficacy between treatment groups. Enrolled patients should include male and female pediatric patients with a clinical diagnosis of bacterial conjunctivitis and a bacteria positive conjunctival culture.

Study Endpoints:
The primary endpoint should be clearing of the infection based on an external ophthalmologic examination. Additionally, conjunctival cultures must be taken between 2 and 10 days after the start of treatment.

Age Groups:
At least 100 culture positive patients between the ages of 0 and 1 month should be enrolled in the trial.

Drug Information:
Moxifloxacin hydrochloride, in an appropriate formulation, should be compared to a concurrent control.

Labeling:
Appropriate sections of the label may be changed to incorporate the findings of the study.

Format of Report To Be Submitted:
A full study report, not previously submitted to the Agency and addressing the issues outlined in this request, should be provided with a full analysis, assessment, and interpretation.

Timeframe:
The report of the above study must be submitted to the Agency on or before October 1, 2002. Please keep in mind that pediatric exclusivity only extends existing patent protection or exclusivity that has not expired or been previously extended at the time you submit your reports of the studies in response to this Written Request.

Please submit the protocol for the above study to an investigational new drug application (IND) and clearly mark your submission **"PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY"** in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission **"PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission.

The report of this study should be submitted as a new NDA or as a supplement to an approved NDA, with the proposed labeling changes you believe would be warranted based on the data derived from this study. When submitting the report, please clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS-PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183) or mail/messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, Maryland 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits for the pediatric population.

If you have any questions, please contact Joanne Holmes, M.B.A., Clinical Reviewer, at (301) 827-2090.

Sincerely,

/S/

Robert DeLap, M.D., Ph.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

CONSULTATION RESPONSE

DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: January 28, 2002	**DUE DATE:** March 15, 2003	**ODS CONSULT #:** 02-0191-1

TO: Lee Simon
Director, Division of Anti-Inflammatory, Analgesic and Ophthalmologic Drug Products
HFD-550

THROUGH: Micheal Puglisi
Project Manager
HFD-550

PRODUCT NAME:	**NDA SPONSOR:**
Vigamox (Moxifloxacin Ophthalmic Solution) 0.5% **NDA:** —	Alcon Inc.

SAFETY EVALUATOR: Denise P. Toyer, Pharm.D.

SUMMARY: In response to a consult from the Division of Ophthalmic Drug Products (HFD-510), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name "Vigamox" to determine the potential for confusion with approved proprietary and established names as well as ending names.

RECOMMENDATIONS:

1. DMETS has no objection to the use of the proprietary name Vigamox.
2. DMETS recommends implementation of the labeling revision outlined in Section III of this review.
3. DDMAC finds the proprietary name acceptable from a promotional perspective.

APPEARS THIS WAY
ON ORIGINAL

Carol Holquist, RPh
Deputy Director,
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 **Fax: (301) 443-9664**

Jerry Phillips, RPh
Associate Director
Office of Drug Safety
Center for Drug Evaluation and Research
Food and Drug Administration

Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; Parklawn Rm. 6-34
Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: March 3, 2003

NDA # [redacted]

NAME OF DRUG: Vigamox
(Moxifloxacin Ophthalmic Solution) 0.5%

NDA HOLDER: Alcon Inc

This review contains information that is provided by IMS Health National Prescription Audit plus (on-line) and is not to be used outside of the FDA without prior clearance by IMS Health. A minimum of 2 weeks is required for clearance by IMS Health.

I. INTRODUCTION:

The Division of Medication Errors and Technical Support (DMETS) reviewed the proprietary names [redacted], submitted by the Division of Anti-Inflammatory, Analgesic and Ophthalmologic Drug Products (DAAODP) for Moxifloxacin Ophthalmic Solution 0.5%. DMETS did not recommend use of [redacted]. The sponsor, Alcon Inc., submitted Vigamox as an alternative. This consult was written in response to a request from DAAODP, to review the proprietary name Vigamox, regarding potential name confusion with other proprietary/established drug names.

PRODUCT INFORMATION

Vigamox is the proposed proprietary names for Moxifloxacin Ophthalmic Solution, 0.5 % which is indicated for the treatment of bacterial conjunctivitis caused by susceptible strains of [redacted] microorganisms. The recommended dosage is to instill one drop in the affected eye(s) three times daily for [redacted] days. This product will be supplied in a [redacted] dispenser.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts[1,2] as well as several FDA databases[3] for existing drug names which sound-alike or look-alike to "Vigamox" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted.[4] The Saegis[5] Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name "Vigamox." Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. The members of this panel include DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. The Expert Panel identified Wymox, Diamox, Vioxx, Zyvox, Vermox, Volmax, and Vaginex as having the potential for confusion with "Vigamox." These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

2. DDMAC did not have concerns about the name Vigamox with regard to promotional claims.

[1] MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.
[2] Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.
[3] The Established Evaluation System [EES], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.
[4] WWW location http://www.uspto.gov/main/trademarks.htm
[5] Data provided by Thomson & Thomson's SAEGIS ™ Online Service, available at www.thomson-thomson.com

Table 1
Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

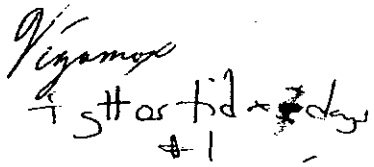
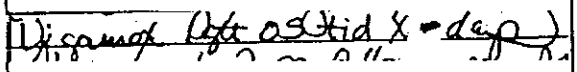
Product Name	Dosage (mg) established name	Usual condition	Other
Vigamox	Moxifloxacin Ophthalmic Solution 0.5%	Instill one drop in affected eye three times a day for [redacted]	
Wymox	Amoxicillin Suspension: 125 mg/5 mL and 250 mg/5 mL	125 mg – 500 mg three times a day	LA/SA
Diamox	Acetazolamide Tablets: 125 mg and 250 mg Extended-release Sequels: 500 mg Injection: 500 mg	Glaucoma: 250 mg to 1 gram daily in divided doses	LA/SA
Vioxx	Rofecoxib Tablets: 12.5 mg, 25 mg, and 50 mg Suspension: 12.5 mg/5 mL and 25 mg/5 mL	Rheumatoid Arthritis: 25 mg every day Dysmenorrhea Pain: 50 mg every day	SA
Zyvox	Linezolid Tablets: 400 mg and 600 mg Injection: 200 mg/100 mL, 300 mg/200 mL, and 400 mg/300 mL Suspension: 100 mg/5 mL	400 – 600 mg every 12 hours depending upon the organism being treated	SA
Vermox	*Mebendazole* Chewable Tablets: 100 mg	*Pinworm: 100 mg one time* Whipworm, Roundworm, and Hookworm: 100 mg two times a day for 3 days	SA
Volmax	Albuterol Sulfate Extended-release Tablets: 4 mg and 8 mg	4 mg – 8 mg every 12 hours	SA
Vaginex	Hydrocortisone Acetate 1% Cream 30 grams (per www.Familymeds.com)	Apply to affected area no more than 3 to 4 times a day	
	Tripelennamine Cream 30 grams (per Electronic Facts & Comparison)	Apply externally to vaginal area 3 to 4 times a day	LA

* Frequently used, not all-inclusive.
** L/A (look-alike), S/A (sound-alike)

B. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Vigamox with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 105 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Vigamox (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

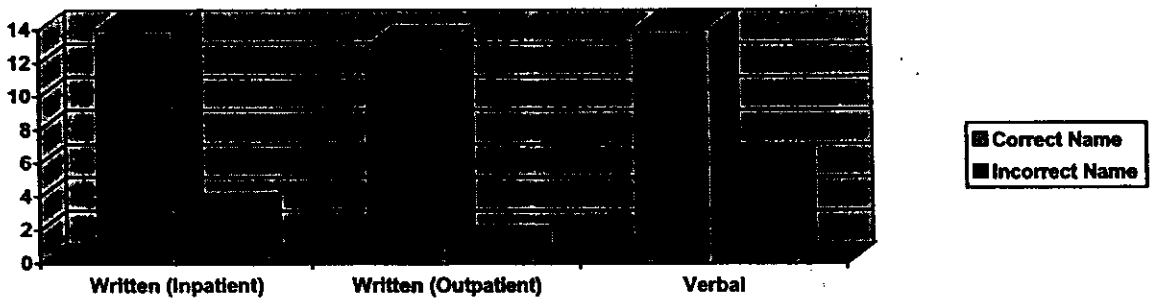
HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: 	The second prescription is for Vigamox. Directions 1 drop in the right eye three times a day for ___ days dispense 1 bottle
Inpatient RX: 	

2. Results:

The results are summarized in Table I.

Table I

Study	# of Participants	# of Responses (%)	Correctly Interpreted	Incorrectly Interpreted
Written Inpatient	35	17 (49%)	14 (82%)	3 (18%)
Written Outpatient	31	14 (45%)	13 (93%)	1 (7%)
Verbal	39	20 (51%)	14 (70%)	6 (30%)
Total	106	51 (48%)	41 (80%)	10 (20%)



In the written inpatient study 3 of 17 (18%) participants interpreted "Vigamox" incorrectly. The incorrect interpretations were Viamox, Vicamox, and Visamax. None of the misinterpreted names were similar to a currently approved product.

In the written outpatient study only one participant (7%) incorrectly misinterpreted "Vigamox." The incorrect misinterpretation was Vizamaz. This name is not similar to a currently approved product.

In the verbal study 6 of 20 (30%) participants interpreted "Vigamox" incorrectly. The majority of the incorrect name interpretations were phonetic variations of "Vigamox." These include Migomox (1), Vegamox (1), Vigamax (1), Vigimox (1), Vigmox (1), and Zigamox (1). None of the six misinterpreted names were similar to a currently approved product.

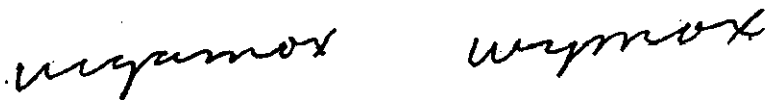
3. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Vigamox, the primary concerns raised were related to seven sound and/or look-alike names: Wymox, Diamox, Vioxx, Zyvox, Vermox, Volmax, and Vaginex.

DMETS conducted prescription studies to simulate the prescription ordering process. There was no confirmation that Vigamox could be confused with Wymox, Diamox, Vioxx, Zyvox, Vermox, Volmax, and Vaginex. The majority of the responses were either phonetic or spelling misinterpretations of the drug name Vigamox.

Wymox may sound or look like Vigamox depending upon how they are scripted or pronounced. Vigamox is an antibiotic used for the treatment of various infections that are susceptible to amoxicillin. Both Wymox and Vigamox begin with letters (w vs. v) that look similar when scripted (see below). The names also end with the same three letters 'mox' which may contribute to the look and sound-alike characteristics. Wymox and Vigamox also have overlapping dosing intervals (three times a day). However, there are some differences between the two names. The hard sound of the letter 'g' in Vigamox helps to distinguish the two products when pronounced. The products have different routes of administration (oral vs. ophthalmic) and dosage forms (oral suspension vs. solution). Additionally, the products do not have overlapping strengths (250 mg and 500 mg vs. 0.5%). Thus prescriptions for Wymox will always require that the strength be indicated, whereas Vigamox prescriptions may be prescribed without indicating a strength. The differences between Wymox and Vigamox will help to decrease the potential for name confusion.

VIGAMOX **WYMOX**



Diamox and Vigamox have sound and look alike similarities. Both names contain three syllables. The ending letters of each name (mox) are identical which increases the look and sound-alike similarities. However, the two beginning syllables (Dia vs. Viga) of both names are distinct when pronounced, especially the 'g' sound in Vigamox. This helps to decrease the sound-alike similarities. The 'g' in Vigamox requires a downstroke when scripted which, also helps to decrease the look-alike similarities (see page 7). Differences between the two products include the route of administration (oral vs. ophthalmic) and dosage form (tablet, capsule, and lyophilized powder vs. solution). Although the dosing intervals may overlap (three times a day), the products are available in different strengths (125 mg, 250 mg, and 500 mg vs. 0.5%). The differences in the beginning letters of both

names and the available strengths will help to minimize the potential for name confusion between Diamox and Vigamox.

Vioxx and Zyvox both share sound-alike characteristics with Vigamox. When pronounced, the endings of the names are identical (ox). However, Vioxx and Zyvox are two syllable names whereas Vigamox contains three syllables. The additional syllable in Vigamox, along with the pronunciation of the second syllable (ga) helps to distinguish these names. Additionally, Vioxx and Zyvox are both available in multiple strengths (12.5 mg, 25 mg, and 50 mg vs. 100 mg, 200 mg, 300 mg, and 600 mg) whereas Vigamox is only available in one single strength (0.5%). Prescriptions for Vigamox may omit the strength. In contrast Vioxx and Zyvox prescriptions will require that a strength be noted prior to dispensing. These differences will help to minimize the potential for name confusion between Vioxx and Vigamox or Zyvox and Vigamox.

Vermox and Vigamox may sound alike when pronounced. Both names begin and end with identical letters (V and mox). This increases the sound-alike characteristics. However, when the first and second syllables of Vigamox are combined, the sound becomes more distinct (Viga vs. Ver). There are additional differences between Vermox and Vigamox. The dosing interval (daily or twice a day vs. three times a day), the route of administration (oral vs. ophthalmic), and the dosage form (tablet vs. solution) are different. Differences in the beginning sounds of Vermox and Vigamox along with the product differences may help to decrease potential name confusion.

Volmax and Vigamox may sound-alike when pronounced. Both names begin with the same letter (V). The last syllable of each name (mox vs. max) may sound alike depending upon how they are pronounced. However, Volmax contains two syllables while Vigamox contains three syllables. The extra syllable in Vigamox also helps to distinguish the two product names when they are pronounced. Volmax is available in two strengths (4 mg and 8 mg) whereas Vigamox is only available in a single strength (0.5%). Prescriptions for Volmax will always require that the strength be indicated which will help to differentiate the two products. The differences between Volmax and Vigamox will help to decrease the potential for sound-alike confusion of these two products.

Vaginex and Vigamox may look-alike depending upon how they are scripted (see page 8). Vaginex, is listed in the electronic version of Facts and Comparison, Micromedex, and www.rx.com as containing the active ingredient Tripelennamine. A search of the COMIS database indicates that the last annual report received, from Novartis, for Vaginex (Tripelennamine) was in 1987. The NDA is not listed in the electronic Orange Book either. The Division of Over-the-Counter Drug Products received a request for withdrawal of the NDA in 1989. Although Vaginex is no longer available as Tripelennamine Cream, the proprietary name Vaginex is listed at Internet drug stores (e.g., www.familymeds.com and www.walgreens.com). The listed products are indicated for external feminine itching and contain the active ingredient hydrocortisone acetate (HC) 1% or a combination of Benzocaine 20% and Resorcinol 3%.

Both Vaginex and Vigamox have the same dosing intervals (three times a day). They have different routes of administration (topical vs. ophthalmic) and dosage forms (cream vs. solution). Although Vaginex is an OTC product and Vigamox

is available by prescription there is a potential for name confusion. This scenario is more likely to occur in an outpatient setting. For example, some practitioners may give patients prescriptions for OTC products as reminders or they may unknowingly write a prescription for a product, not realizing that it is available over the counter. Thus a prescription for Vigamox, Dispense #1, Use as directed could potentially be interpreted as Vaginex.

Vaginex	Vigamox
Vaginex	Vigamox

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

The Vigamox labels and labeling were submitted in draft format, which did not allow for a complete DMETS review. However, DMETS has attempted to focus on safety issues relating to possible medication errors and identified the following areas of possible improvement, which might minimize potential user error.

A. CARTON LABELING (3 mL Trade Size)

The expression of strength should be expressed in terms of the active moiety consistent with FDA and USP labeling standards. In this regard please revise as follows:

FRONT PANEL

Vigamox
(Moxifloxacin Ophthalmic Solution)
0.5%*

BACK OR SIDE PANEL

NOTE: *The quantitative amount of Moxifloxacin HCL could be confusing and should not be listed here.*

B. CONTAINER LABEL (3 mL Trade Size)

See Comment A.

C.

1.

2.

D.

1.

E. PACKAGE INSERT LABELING

1. In the Description Section, we recommend that the active ingredient be expressed in percent and mg/mL (not 5,000 µg/mL).

2. In the How Supplied Section. e since this is a

IV. RECOMMENDATIONS:

A. DMETS has no objection to the proprietary name Vigamox.

B. DMETS recommends implementation of the labeling revision outlined in Section III of this review.

C. DDMAC finds the proprietary name acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Sammie Beam, project manager, at 301-827-3242.

Denise P. Toyer, Pharm.D.
Safety Evaluator/Team Leader
Division of Medication Errors and Technical Support

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/s/

Denise Toyer
3/19/03 01:24:43 PM
PHARMACIST

Carol Holquist
3/21/03 08:01:49 AM
PHARMACIST

Jerry Phillips
3/21/03 10:48:53 AM
DIRECTOR

APPEARS THIS WAY
ON ORIGINAL

5 Page(s) Withheld

_____ § 552(b)(4) Trade Secret / Confidential

✓ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Peter Silas, M.D.
Wee Care Pediatrics
1580 West Antelope Drive, Suite 100
Layton, Utah 84041

FEB 20 2003

Dear Dr. Silas:

On January 9-13, 2003, Messrs. Thaddeus Steinke and Blake Jensen, representing the Food and Drug Administration (FDA), conducted an investigation and met with you to review your conduct of a clinical investigation (protocol #C-01-034 entitled: "An Evaluation of the Safety and Clinical Improvement Rate of Ciprofloxacin Ophthalmic Solution 0.3% (CILOXAN) and Moxifloxacin Ophthalmic Solution 0.5% in Neonates with Presumed Bacterial Conjunctivitis") of the investigational drug moxifloxacin, performed for Alcon. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to monitor the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of those studies have been protected.

From our review of the establishment inspection report and the documents submitted with that report, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations and the protection of human subjects. We are aware that at the conclusion of the inspection, Messrs. Steinke and Jensen presented and discussed with you Form FDA 483, Inspectional Observations. The discussion included the nonperformance of protocol-specified conjunctival discharge smears on seven subjects (21 CFR 312.60).

Please make appropriate corrections in your procedures to assure that the finding noted above is not repeated in any ongoing or future studies.

We appreciate the cooperation shown Investigators Steinke and Jensen during the inspection. Should you have any questions or concerns regarding this letter or the inspection, please contact me by letter at the address given below.

Sincerely,

/S/

Antoine El-Hage, Ph.D.
Associate Director
Good Clinical Practice Branch I & II, HFD-46/47
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place, Room 125
Rockville, MD 20855

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Angela Kothe, Ph.D.	**From:** Mike Puglisi
Fax: 817-551-4630	**Fax:** 301-827-2531
Phone:	**Phone:** 301-827-2522
Pages: 2 (incl. cover)	**Date:** February 3, 2003
Re: Clinical Information Request re: [redacted] (& NDA 21-598)	

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

• **Comments:**

Angela-

Here's another information request from our Medical Officer concerning [redacted] (& 21-598) for moxifloxacin ophthalmic solution. Please let me know if you have any questions about this request.

-Mike

Medical Officer's Request for Information

Organisms that are not speciated will be excluded from the INDICATIONS AND USAGE section of the label. Please provide the specie(s) for the following organisms:

1) Protocol C-00-55, Module 5, Volume 1.16, Technical Report, pages 56-61 of 64:

   Other viridans Streptococcus – Please explain the species/subspecies that the category includes.

   Haemophilus sp. nov. "alconae"

2) Protocol C-00-46, Module 5, Volume 1.20, Technical Report, pages 3-12 of 78:

   Acinetobacter spp.

3) Protocol C-01-34, Module 5, Volume 1.25, Technical Report, pages 3-10 of 70:

   Viridans Streptococcus

   Haemophilus sp. nov. 2

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/s/

Michael Puglisi
2/3/03 04:24:53 PM
CSO

Michael Puglisi
2/3/03 04:28:11 PM
CSO

APPEARS THIS WAY
ON ORIGINAL

Fax

Division of Anti-Inflammatory, Analgesic, Ophthalmic Drug Products
Center for Drug Evaluation and Research, HFD-550
Parklawn Building
5600 Fishers Lane, Rockville, MD 20857

To: Angela Kothe, Ph.D.	**From:** Mike Puglisi
Fax: 817-551-4630	**Fax:** 301-827-2531
Phone:	**Phone:** 301-827-2522
Pages: 1 (incl. cover)	**Date:** January 22, 2003
Re: Clinical Information Request re: [redacted] & NDA 21-598)	

☐ **Urgent** ☐ **For Review** ☐ **Please Comment** ☐ **Please Reply** ☐ **Please Recycle**

• **Comments:**

Angela-

Here's an information request from our Medical Officer concerning [redacted] (& 21-598) for moxifloxacin ophthalmic solution. Please let me know if you have any questions about this request.

-Mike

Medical Officer's Request for Information

- Protocol C-00-46, Module 5, Volume 1.18, Section 16.1.4, page 661 states that the section includes "brief CVs or equivalent summaries of training and experience" of Investigators and other important participants in the study.

  Please identify where this information may be found in the submission. If the information was not included in the original submission, please submit.

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/s/

Michael Puglisi
1/22/03 01:39:41 PM
CSO

Michael Puglisi
1/22/03 01:42:35 PM
CSO

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

FILING REVIEW ISSUES IDENTIFIED

NDA 21-598

Alcon, Inc.
c/o Alcon Research, Ltd.
Attention: Angela C. Kothe, Ph.D.
Assistant Director, Regulatory Affairs
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Dr. Kothe:

Please refer to your October 14, 2002, new drug applications (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Moxifloxacin Hydrochloride Ophthalmic Solution, 0.5%

We have completed our filing review of your application and have identified the following issue:

> The submitted primary efficacy analysis failed to show a difference between treatment groups.

We are providing the above comments to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application.

A response to this letter is not expected and any such response may not be reviewed during the current review cycle.

If you have any questions, call Michael Puglisi, Regulatory Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}
Carmen DeBellas, R.Ph.
Chief, Project Management Staff
Division of Anti-Inflammatory, Analgesic,
and Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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/s/

Carmen DeBellas
12/23/02 04:37:09 PM

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✓ § 552(b)(5) Deliberative Process

_____ § 552(b)(5) Draft Labeling

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Alcon Universal, Ltd.
c/o Alcon Laboratories Inc.
Attention: Angela C. Kothe, OD Ph.D.
Assistant Director, Regulatory Affairs
6201 South Freeway
Fort Worth, Texas 76134-2099

Dear Dr. Kothe:

Please refer to your correspondence dated July 31, 2002, requesting changes to FDA's Written Request dated June 26, 2000, and amended August 3, 2001, for pediatric studies for moxifloxacin hydrochloride.

We have reviewed your proposed changes and are amending the below listed sections of the Written Request. All other terms stated in our Written Request dated June 26, 2000, as amended August 3, 2001, remain the same.

Timeframe

Reports of the studies that meet the terms of the Written Request dated June 26, 2000, as amended August 3, 2001, and amended by this letter must be submitted to the Agency on or before January 1, 2003, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Submit reports of the studies with your New Drug Application (NDA) with the proposed labeling changes you believe are warranted based on the data derived from these studies. When submitting the reports, clearly mark your submission **"SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED"** in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. In addition, send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773. If you choose, you may send a copy of the cover letter by U.S. mail to the Director, Office of Generic Drugs, HFD-600, 5600 Fishers Lane, Rockville, MD, 20857.

If you wish to discuss any amendments to this Written Request, submit proposed changes and the reasons for the proposed changes to your application. Clearly mark submissions of proposed changes to this request **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. We will notify you in writing if we agree to any changes to this Written Request.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits to the pediatric population.

If you have any questions, call Lori M. Gorski, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Jonca C. Bull, M.D.
Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

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/s/

Jonca Bull
9/6/02 06:46:34 PM

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Alcon Univeral, Ltd.
c/o Alcon Laboratories, Inc.
Attention: Scott Krueger
Senior Director, Regulatory Affairs
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Mr. Krueger:

Reference is made to FDA's June 26, 2000, Written Request for pediatric studies for moxifloxacin hydrochloride.

We are amending the below listed sections of the Written Request. All other terms stated in our Written Request issued on June 26, 2000, remain the same.

Indication/Objective:
The primary objective of the study should be to evaluate the safety and the clinical improvement rate between treatment groups. Enrolled patients should include male and female pediatric patients with a clinical diagnosis of presumed bacterial conjunctivitis.

Age Groups
Patients should be between the ages of 0 and 1 month. At least 100 culture positive patients or 200 patients with red eyes should be enrolled in the trial.

The report of the study that meets the terms of the Written Request dated June 26, 2000, as amended by this letter must be submitted to the Agency on or before October 1, 2002, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

Please submit the protocol for the above study to an investigational new drug application (IND) and clearly mark your submission, "PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Please clearly mark your submission, "PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission.

The report of the study should be submitted as a new drug application or as a supplement to an approved NDA with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the report, please clearly mark your submission "SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. Please also send a copy of the cover letter of your submission, via fax (301-594-0183), mail, or messenger to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, please submit proposed changes and the reasons for the proposed changes to your application. Submissions of proposed changes to this request should be clearly marked "PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES" in large font, bolded type at the beginning of the cover letter of the submission. You will be notified in writing if any changes to this Written Request are agreed upon by the Agency.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits to the pediatric population.

If you have any questions, contact Lori M. Gorski, Regulatory Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Jonca C. Bull, M.D.
Acting Director
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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✓ § 552(b)(4) Trade Secret / Confidential

_____ § 552(b)(5) Deliberative Process

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