CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

050616sOrig1s018

Trade Name:	**TobraDex, Ophthalmic Ointment**
Generic or Proper Name:	(Tobramycin and Dexamethasone)
Sponsor:	**Novartis**
Approval Date:	December 11, 2002
Indication:	TOBRADEX Ophthalmic Ointment is indicated for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacteria ocular infection or a risk of bacterial ocular infection exists.

CENTER FOR DRUG EVALUATION AND RESEARCH

050616sOrig1s018

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Reviews / Information Included in this NDA Review.

Approval Letter	**X**
Other Action Letters	
Labeling	
REMS	
Summary Review	
Officer/Employee List	
Office Director Memo	
Cross Discipline Team Leader Review	
Clinical Review(s)	
Product Quality Review(s)	**X**
Non-Clinical Review(s)	
Statistical Review(s)	
Clinical Microbiology / Virology Review(s)	**X**
Clinical Pharmacology Review(s)	
Other Reviews	
Risk Assessment and Risk Mitigation Review(s)	
Proprietary Name Review(s)	
Administrative/Correspondence Document(s)	

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050616sOrig1s018

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 13-422/S-034 NDA 50-592/S-031 NDA 50-628/S-004
NDA 19-079/S-023 NDA 50-616/S-018

Alcon Laboratories, Inc.
Attention: Norma J. Schafer
Regulatory Affairs Analyst
6201 South Freeway
Fort Worth, TX 76134-2099

Dear Ms. Schafer:

Please refer to your supplemental new drug applications dated June 13, 2002, submitted under the Federal Food, Drug, and Cosmetic Act for the following:

We also acknowledge receipt of your submission dated October 21, 2002.

13-422/S-034	MAXIDEX (dexamethasone ophthalmic solution) 0.5%
19-079/S-023	FLAREX (fluorometholone acetate ophthalmic suspension)
50-592/S-031	TOBRADEX (tobramycin and dexamethasone ophthalmic solution)
50-616/S-018	TOBRADEX (tobramycin and dexamethasone ophthalmic ointment)
50-628/S-004	TOBRASONE (tobramycin and fluorometholone acetate ophthalmic suspension)

These "Changes Being Effected" supplemental new drug applications provide for a change in biological indicator incubation time to assess sterilization of the drug substance.

We have completed the review of these supplemental applications, and they are approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Raphael R. Rodriguez, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}
Linda L. Ng, Ph.D.
Chemistry Team Leader for the
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, (HFD-550)
DNDC III, Office of New Drug Chemistry
Center for Drug Evaluation and Research

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/s/

Linda Ng
12/11/02 03:31:20 PM

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050616sOrig1s018

PRODUCT QUALITY REVIEW(S)

CHEMIST'S REVIEW # 1	**1. ORGANIZATION** HFD-550 DAAODP	**2. NDA NUMBER** 13-422
3. NAME AND ADDRESS OF APPLICANT *(City and State)* Alcon Research, Ltd. 6201 South Freeway Forth Worth, Texas 76134-2099		**4. AF NUMBER** **5. SUPPLEMENT(S)** NUMBER(S) DATES(S) SCS-034 6/13/02 **lead bundle supplement**
6. NAME OF DRUG: Maxidex® (dexamethasone ophthalmic suspension) 0.1%.	**7. NONPROPRIETARY NAME:** Dexamethasone	
8. SUPPLEMENT PROVIDES FOR: Change the incubation time for biological indicators (from current 7 days to 4 days) for routine production cycles. CBE 30 supplement		**9. AMENDMENT(S), REPORT(S), ETC.** NUMBER(S) DATE(S) 13-422/SCS-034 10/21/2002 17-469/SCS-030 10/21/2002 19-079/SCS-023 10/21/2002 50-023/SCS-023 10/21/2002 50-065/SCS-041 10/21/2002 50-592/SCS-031 10/21/2002 50-616/SCS-018 10/21/2002 50-628/SCS-004 10/21/2002
10. PHARMACOLOGICAL CATEGORY Anti-inflammatory	**11. HOW DISPENSED** RX X OTC	**12. RELATED IND/NDA/DMF** NUMBER(S) DATE(S)
13. DOSAGE FORM(S) Suspension	**14. POTENCY** 0.1%	17-469/SCS-030 6/13/2002 19-079/SCS-023 6/13/2002 50-023/SCS-023 6/13/2002 50-065/SCS-040 6/13/2002 50-592/SCS-031 6/13/2002 50-616/SCS-017 6/13/2002 50-628/SCS-004 6/13/2002
15. CHEMICAL NAME AND STRUCTURE		**16. RECORDS AND REPORTS** CURRENT YES__NO REVIEWED YES__NO

17. COMMENTS:

a. First micro review was done on 9/3/02 and as a result, an IR letter was forwarded to the applicant on 10/18/02.
b. Applicant responded to the micro deficiencies in amendment dated 10/21/02.
c. Second micro review dated 11/26/02 recommended these supplements for approval.

18. RRECOMMENDATION:

a. From CMC standpoint, and based on micro review result, these supplements are approved.
b. Comment listed in the draft chemistry deficiencies and comments letter should be forwarded to the applicant with the approval letter.

cc:
Orig. NDA 13-422/SCS-034
HFD-550/div. File
HFD-550/HKhorshidi
HFD-550/LNg
HFD-550/WChambers
HFD-550/RRodriquez
R/D Init. by:_LNg_
F/T by: HKhorshidi
doc # N:\NDA\13/422\SCS-034\Chem\2002. 12. 02 REV

19. REVIEWER NAME:	**SIGNATURE**	**DATE COMPLETED**
Hossein S. Khorshidi		

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/s/

Hossein Khorshidih
12/6/02 10:41:12 AM
CHEMIST

Linda Ng
12/6/02 05:48:44 PM
CHEMIST
PM to prepare an AP letter

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

050616sOrig1s018

CLINICAL MICROBIOLOGY/VIROLOGY REVIEW(S)

Product Quality Microbiology Review
Consult review for HFD-550

3 SEPTEMBER 2002

NDA/ANDA:	NDA 13-422/SCS034 & supplements to 7 other NDAs listed in Tables 1.
Name of Drug:	Maxidex®
Review Number:	1
Submission Date:	June 13, 2002
Applicant:	Alcon
Name of Reviewer:	Vinayak Pawar
Conclusion:	Based on the data provided, the NDA applications are approvable pending resolution of the issues listed in Section H of Product Quality Microbiology Assessment.

Product Quality Microbiology Data Sheet

A. 1. **NDA:** 13-422/SCS034 & supplements to other NDAs, ANDAs and AADAs listed in Tables 1 & 2.

2. **REVIEW NUMBER:** 1

3. **REVIEW DATE:** 3 September, 2002

4. **TYPE OF SUPPLEMENT:** SCS

5. **SUPPLEMENT PROVIDES FOR:** change in [redacted] (b) (4)

6. **APPLICANT/SPONSOR:**

Name: ALCON
Representative: Norma J, Schafer
Telephone: 817-551-8568

7. **MANUFACTURING SITE:** No change

8. **DRUG PRODUCT NAME:**
Proprietary: Maxidex®
Non-proprietary: NA
Drug Priority Classification: NA

9. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** NA

10. **METHOD (S) OF STERILIZATION:** No change

11. **PHARMACOLOGICAL CATEGORY:** NA

B. 1. **DOCUMENT/LETTER DATE:** June 13, 2002
2. **RECEIPT DATE:** June 14, 2002
3. **CONSULT DATE:** June 18,2002
4. **DATE OF AMENDMENTS:** NA
5. **ASSIGNED FOR REVIEW:** August 23, 2002
6. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** The consult requests review of CBE-30 Day supplement SCS034 to NDA13-422 & other supplements to NDA [redacted] (b) (4) A single volume of the supplemental application was

submitted for review. No changes are requested for the manufacturing process or the sterilization of the product.

Table 1. List of NDAs Affected

NDAs	
PRODUCT	**NUMBER**
MAXIDEX®	13-422/SCS034
ECONOPRED® PLUS	17-469/SCS030
FLAREX®	19-079/SCS023
MAXITROL®	50-023/SCS023
MAXITROL®	50-065/SCS041
TOBRADEX®	50-592/SCS031
TOBRADEX®	50-616/SCS018
TOBRAFLEX™	50-628/SCS004

Executive Summary

I. Recommendations

(b) (4)

[redacted]

B. Recommendation on Phase 4 Commitments and/or Agreements, if Approvable NA

II. Summary of Microbiology Assessments

(b) (4)

[redacted]

B. Brief Description of Microbiology Deficiencies

See Section H of Product Quality Microbiology Assessment.

C. Assessment of Risk Due to Microbiology Deficiencies-

Minimal

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

Vinayak Pawar/3 September, 2002
Peter H. Cooney/

C. CC Block

cc:
Original NDA 13-422/SCS034 & Others
HFD-550/Division File/Raphael Rodriguez

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/s/

Vinayak Pawar
9/5/02 10:50:30 AM
MICROBIOLOGIST

Peter Cooney
9/5/02 02:19:56 PM
MICROBIOLOGIST