CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

200738Orig1s000

CHEMISTRY REVIEW(S)

NDA 200-738

LOTEMAX®
(loteprednol etabonate ophthalmic ointment) 0.5%

Bausch & Lomb Incorporated

Lin Qi
Division of Anti-Infective and Ophthalmology Product

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A. Recommendation and Conclusion on Approvability: 7

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. 7

An "Acceptable" site recommendation from the Office of Compliance has been made. 7

Therefore, from the CMC perspective, this NDA is recommended for *approval*. 7

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 7

II. Summary of Chemistry Assessments 7

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An "Acceptable" site recommendation from the Office of Compliance has not been made on April 12, 2011 (See Attachment). Therefore, from the CMC perspective, this NDA is *recommended for approval*. 8

III. Administrative 9

{See signatures in DARRTS} 9

A. Reviewer's Signature 9

B. Endorsement Block 9

C. CC Block: Listed in DARRTS 9

Chemistry Review Data Sheet

1. NDA 200-738

2. REVIEW #: 3

3. REVIEW DATE: April 12, 2011

4. REVIEWER: Lin Qi

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	12/22/2009
Amendment	1/26/2010
Amendment	5/27/2010
Amendment	7/21/2010
Amendment	9/21/2010

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	1/24/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Bausch and Lomb Incorporated
Address:	7 Giralda Farms, Suite 1001 Madison, NJ 07940
Representative:	Michael Bailey
Telephone:	973-360-6397

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: LOTEMAX
b) Non-Proprietary Name (USAN): loteprednol etabonate
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b) (1)

10. PHARMACOL. CATEGORY: Corticosteroid (Anti-inflammation)

11. DOSAGE FORM: Ointment

12. STRENGTH/POTENCY: 0.5%

13. ROUTE OF ADMINISTRATION: Ophthalmic

14. Rx/OTC DISPENSED: _X__Rx ___OTC

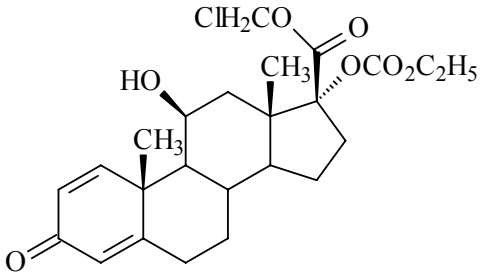
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Names: Chloromethyl 17α-[(ethoxycarbonyl)oxy]- 11β-hydroxy-3-oxoandrosta-1,4-diene-17β-carboxylate



Molecular formula: $C_{24}H_{31}ClO_7$
Molecular weight: 466.96

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II	(b) (4)	Loteprednol Etabonate	1	Adequate	Aug 19, 2010 (L.Qi)	LOA 9/3/2009
(b) (4)	III	(b) (4)	(b) (4)	1	Adequate	Aug 19, 2010 (L.Qi)	LOA 2/5/2008

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	32,432	Loteprednol Etabonate
IND	36,209	Loteprednol Etabonate and Tobramycin Ophthalmic Suspension, 0.5%/0.3%
(b) (4)		
NDA	20-583	Lotemax ® (loteprednol etabonate ophthalmic suspension, 0.5%)
NDA	20-803	Alrex® (loteprednol etabonate ophthalmic suspension, 0.2%)
NDA	50-804	Zylet® (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension)

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	Acceptable	4/12/2011	M Stock
Pharm/Tox	Acceptable	7/19/2010	Conrad Chen
Biopharm			
LNC			
Methods Validation	NA	8/23/2010	Lin Qi
OPDRA			
EA	Acceptable	9/22/2010	Lin Qi
Microbiology	Acceptable	7/2/2010	Brian Riley

The Chemistry Review for NDA 200-738

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability:

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product.

An "Acceptable" site recommendation from the Office of Compliance has been made.

Therefore, from the CMC perspective, this NDA is recommended for ***approval***.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, loteprednol etabonate, is a white to off-white powder. It is insoluble in water. Loteprednol etabonate (LE) is the same drug substance as is currently used in LOTEMAX (loteprednol etabonate ophthalmic suspension 0.5%) (NDA 20-583). The drug substance is manufactured and (b) (4) DMF (b) (4) is referenced for drug substance information. (b) (4) The drug substance is tested by Bausch & Lomb Incorporated (B&L) in Tampa, Florida.

The drug product, LOTEMAX (loteprednol etabonate ophthalmic ointment) 0.5%, will be manufactured at the facility in Tampa. In the current formulation, the drug substance is (b) (4) containing mineral oil and white petrolatum (See page 54 for composition). Dr. Brian Riley found that the microbiological information provided in the application is acceptable in his product microbiological review dated July 2, 2010. Each of these excipients is tested to ensure conformance to the current requirements of the USP monograph. The drug product specification is appropriate and includes: Description, Particulate Matter, Metal Particles, Particle Size Distribution, Identification, Assay, Related Substances, (b) (4), Dose Uniformity, Leak Test, Minimum Fill, (b) (4) Sterility, and Endotoxin (See page 69). Bausch & Lomb (B&L) has incorporated residual solvents testing into the specifications for all ingredients used to manufacture Loteprednol Etabonate Ophthalmic Ointment to ensure ICH Q3C limits for the drug product are not

exceeded. Loteprednol Etabonate Ophthalmic Ointment is packaged in 3.5 g and 2.0 g tin tubes with low density polyethylene caps, with a fill volume of 3.5 and 1 g, respectively.

The 3.5 g fill commercial configuration is assigned an expiry period of 18 months at a recommended storage temperature of 15 - 25°C. The 1 g fill physician sample configuration is assigned an expiry of 9 months at a recommended storage temperature of 15 - 25ºC.

B. Description of How the Drug Product is Intended to be Used

The drug product, LOTEMAX (loteprednol etabonate ophthalmic ointment) 0.5%, is indicated for the treatment of post-operative inflammation and pain following ocular surgery. LOTEMAX ointment is a topical ophthalmic ointment. Its administration instruction is "Apply a small amount (approximately ½ inch ribbon) into the conjunctival sac(s) four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period".

C. Basis for Approvability or Not-Approval Recommendation

This application was not recommended for approval in CMC review #2 because of the pending status of establishment evaluation.

An "Acceptable" site recommendation from the Office of Compliance has not been made on April 12, 2011 (See Attachment).

Therefore, from the CMC perspective, this NDA is ***recommended for approval***.

III. Administrative

{See signatures in DARRTS}

A. Reviewer's Signature

_____ _____

Lin Qi, Ph.D. Date
Review Chemist

_____ _____

Linda Ng, Ph.D. Date
CMC Lead

B. Endorsement Block

ChemistName/Date: LQi/April 12, 2011
CMCLeadName/Date: LNg/April 12, 2011
ProjectManagerName/Date: FIzadi/April 12, 2011
ACuff/April 12, 2011

C. CC Block: Listed in DARRTS

5 Page(s) have been Withheld in full as b4 (CCI/TS) immediately following this page

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/s/

LIN QI
04/12/2011

LINDA L NG
04/12/2011

NDA 200-738

LOTEMAX®
(loteprednol etabonate ophthalmic ointment) 0.5%

Bausch & Lomb Incorporated

Lin Qi
Division of Anti-Infective and Ophthalmology Product

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I. Recommendations 7

A. Recommendation and Conclusion on Approvability: 7

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product. 7

However, a recommendation from the Office of Compliance on the site acceptability has not been made as of the date of this review. 7

Therefore, from the CMC perspective, this NDA is *not recommended for approval* until the site acceptability is established. 7

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable 7

II. Summary of Chemistry Assessments 7

A. Description of the Drug Product(s) and Drug Substance(s) 7

B. Description of How the Drug Product is Intended to be Used 8

C. Basis for Approvability or Not-Approval Recommendation 8

However, a recommendation from the Office of Compliance on the site acceptability has not been made as of the date of this review. Therefore, from the CMC perspective, this NDA is *not recommended for approval* until the site acceptability is established. 8

III. Administrative 9

A. Reviewer's Signature 9

B. Endorsement Block 9

C. CC Block: Listed in DARRTS 9

Chemistry Assessment 10

Chemistry Review Data Sheet

1. NDA 200-738

2. REVIEW #: 2

3. REVIEW DATE: April 4, 2011

4. REVIEWER: Lin Qi

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	12/22/2009
Amendment	1/26/2010
Amendment	5/27/2010
Amendment	7/21/2010
Amendment	9/21/2010

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	1/24/2011

7. NAME & ADDRESS OF APPLICANT:

Name:	Bausch and Lomb Incorporated
Address:	7 Giralda Farms, Suite 1001 Madison, NJ 07940
Representative:	Michael Bailey
Telephone:	973-360-6397

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: LOTEMAX
b) Non-Proprietary Name (USAN): loteprednol etabonate
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b) (1)

10. PHARMACOL. CATEGORY: Corticosteroid (Anti-inflammation)

11. DOSAGE FORM: Ointment

12. STRENGTH/POTENCY: 0.5%

13. ROUTE OF ADMINISTRATION: Ophthalmic

14. Rx/OTC DISPENSED: _X__Rx ___OTC

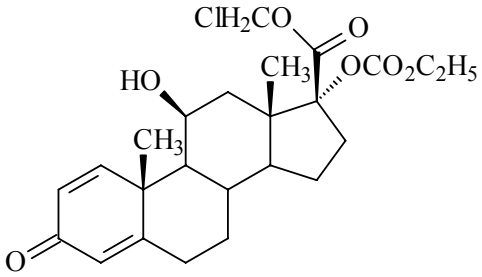
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Names: Chloromethyl 17α-[(ethoxycarbonyl)oxy]- 11β-hydroxy-3-oxoandrosta-1,4-diene-17β-carboxylate



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17. RELATED/SUPPORTING DOCUMENTS:

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18. STATUS:

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EES	Pending	4/7/2011	
Pharm/Tox	Acceptable	7/19/2010	Conrad Chen
Biopharm			
LNC			
Methods Validation	NA	8/23/2010	Lin Qi
OPDRA			
EA	Acceptable	9/22/2010	Lin Qi
Microbiology	Acceptable	7/2/2010	Brian Riley

The Chemistry Review for NDA 200-738

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability:

This NDA has provided sufficient information to assure identity, strength, purity, and quality of the drug product.

However, a recommendation from the Office of Compliance on the site acceptability has not been made as of the date of this review.

Therefore, from the CMC perspective, this NDA is ***not recommended for approval*** until the site acceptability is established.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, loteprednol etabonate, is a white to off-white powder. It is insoluble in water. Loteprednol etabonate (LE) is the same drug substance as is currently used in LOTEMAX (loteprednol etabonate ophthalmic suspension 0.5%) (NDA 20-583). The drug substance is manufactured and (b) (4) DMF (b) (4) is referenced for drug substance information. (b) (4) The drug substance is tested by Bausch & Lomb Incorporated (B&L) in Tampa, Florida.

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C. Basis for Approvability or Not-Approval Recommendation

This application was not recommended for approval in CMC review #1 because of the following pending issues:

1. Satisfactory resolution of the inspectional deficiencies are required before this application may be approved.
2. Satisfactory responses to the following product quality deficiencies regarding the dose uniformity test are required before this application may be approved:
    a. Based on the summary information about the effect of storage time on dose uniformity which was provided in your amendment dated Sep 21, 2010, it is not possible to determine whether the proposed acceptance criteria are appropriate. Please submit the complete dataset from this study, so that the acceptance criteria can be established based on a more thorough analysis.
    b. Please also provide a risk assessment of an adverse impact on safety or efficacy at the dose uniformity ranges that are observed at longer storage times.

In this amendment, appropriate analytical procedures and acceptance criteria were provided on drug product content uniformity. The analytical procedure "Assay and Related Substances by HPLC (C-1689)" was adequately modified to include content uniformity testing. Method validation was updated. Content uniformity results at release and for aged samples support the adequacy of the proposed acceptance criteria of 90-110% of label claim.

However, a recommendation from the Office of Compliance on the site acceptability has not been made as of the date of this review. Therefore, from the CMC perspective, this NDA is ***not recommended for approval*** until the site acceptability is established.

III. Administrative

{See signatures in DARRTS}

A. Reviewer's Signature

_____ _____

Lin Qi, Ph.D. Date
Review Chemist

_____ _____

Linda Ng, Ph.D. Date
CMC Lead

B. Endorsement Block

ChemistName/Date: LQi/Sep 22, 2010
CMCLeadName/Date: LNg/Sep 22, 2010
ProjectManagerName/Date: FIzadi/Sep 22, 2010
ACuff/Sep 22, 2010
JDavid/Sep 22, 2010

C. CC Block: Listed in DARRTS

6 Page(s) have been Withheld in full as b4 (CCI/TS) immediately following this page

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/s/

LIN QI
04/07/2011

LINDA L NG
04/08/2011
Signing on behalf of Stephen Miller, Ph.D.

NDA 200-738

LOTEMAX®
(loteprednol etabonate ophthalmic ointment) 0.5%

Bausch & Lomb Incorporated

Lin Qi
Division of Anti-Infective and Ophthalmology Product

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III. Administrative 9

A. Reviewer's Signature 9

B. Endorsement Block 9

C. CC Block 9

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Chemistry Review Data Sheet

1. NDA 200-738

2. REVIEW #: 1

3. REVIEW DATE: Sep 22, 2010

4. REVIEWER: Lin Qi

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	12/22/2009
Amendment	1/26/2010
Amendment	5/27/2010
Amendment	7/21/2010
Amendment	9/21/2010

7. NAME & ADDRESS OF APPLICANT:

Name:	Bausch and Lomb Incorporated
Address:	7 Giralda Farms, Suite 1001 Madison, NJ 07940
Representative:	Michael Bailey
Telephone:	973-360-6397

Chemistry Review Data Sheet

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: LOTEMAX
b) Non-Proprietary Name (USAN): loteprednol etabonate
c) Code Name/# (ONDC only):
d) Chem. Type/Submission Priority (ONDC only):

- Chem. Type: 3
- Submission Priority: S

9. LEGAL BASIS FOR SUBMISSION: 505 (b) (1)

10. PHARMACOL. CATEGORY: Corticosteroid (Anti-inflammation)

11. DOSAGE FORM: Ointment

12. STRENGTH/POTENCY: 0.5%

13. ROUTE OF ADMINISTRATION: Ophthalmic

14. Rx/OTC DISPENSED: _X__Rx ___OTC

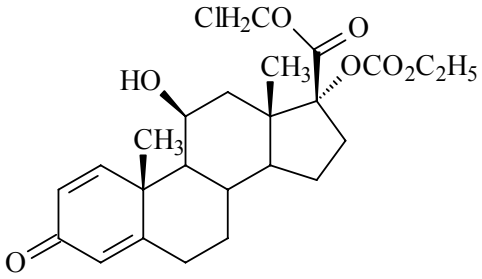
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X___Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Names: Chloromethyl 17α-[(ethoxycarbonyl)oxy]- 11β-hydroxy-3-oxoandrosta-1,4-diene-17β-carboxylate



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Molecular weight: 466.96

17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

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(b) (4)	III	(b) (4)	(b) (4)	1	Adequate	Aug 19, 2010 (L.Qi)	LOA 2/5/2008

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[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
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IND	36,209	Loteprednol Etabonate and Tobramycin Ophthalmic Suspension, 0.5%/0.3%
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NDA	20-583	Lotemax ® (loteprednol etabonate ophthalmic suspension, 0.5%)
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NDA	50-804	Zylet® (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension)

18. STATUS:

ONDC:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Biometrics			
EES	Withhold	9/16/2010	OC
Pharm/Tox	Acceptable	7/19/2010	Conrad Chen
Biopharm			
LNC			
Methods Validation	NA	8/23/2010	Lin Qi
OPDRA			
EA	Acceptable	9/22/2010	Lin Qi
Microbiology	Acceptable	7/2/2010	Brian Riley

The Chemistry Review for NDA 200-738

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability:

This NDA has not provided sufficient information to assure identity, strength, purity, and quality of the drug product. Specifically, data is needed to justify an appropriate acceptance criterion for the dose uniformity test.

A site recommendation of "Withhold" was made by the Office of Compliance, since manufacturing facilities are not in compliance with current good manufacturing practice.

Therefore, from the CMC perspective, this NDA is ***not recommended for approval*** until all pending issues are resolved.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if Approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug substance, loteprednol etabonate, is a white to off-white powder. It is insoluble in water. Loteprednol etabonate (LE) is the same drug substance as is currently used in LOTEMAX (loteprednol etabonate ophthalmic suspension 0.5%) (NDA 20-583). The drug substance is manufactured and (b) (4) DMF (b) (4) is referenced for drug substance information. (b) (4) The drug substance is tested by Bausch & Lomb Incorporated (B&L) in Tampa, Florida.

The drug product, LOTEMAX (loteprednol etabonate ophthalmic ointment) 0.5%, will be manufactured at the facility in Tampa. In the current formulation, the drug substance is (b) (4) containing mineral oil and white petrolatum (See page 54 for composition). Dr. Brian Riley found that the microbiological information provided in the application is acceptable in his product microbiological review dated July 2, 2010. Each of these excipients is tested to ensure conformance to the current requirements of the USP monograph. The drug product specification is appropriate and includes: Description, Particulate Matter, Metal Particles, Particle Size Distribution, Identification, Assay, Related

Substances, (b) (4) Dose Uniformity, Leak Test, Minimum Fill, (b) (4) Sterility, and Endotoxin (See page 69). Bausch & Lomb (B&L) has incorporated residual solvents testing into the specifications for all ingredients used to manufacture Loteprednol Etabonate Ophthalmic Ointment to ensure ICH Q3C limits for the drug product are not exceeded. Loteprednol Etabonate Ophthalmic Ointment is packaged in 3.5 g and 2.0 g tin tubes with low density polyethylene caps, with a fill volume of 3.5 and 1 g, respectively. The 3.5 g fill commercial configuration is assigned an expiry period of 18 months at a recommended storage temperature of 15 - 25°C. The 1 g fill physician sample configuration is assigned an expiry of 9 months at a recommended storage temperature of 15 - 25ºC.

B. Description of How the Drug Product is Intended to be Used

The drug product, LOTEMAX (loteprednol etabonate ophthalmic ointment) 0.5%, is indicated for the treatment of post-operative inflammation and pain following ocular surgery. LOTEMAX ointment is a topical ophthalmic ointment. Its administration instruction is "Apply a small amount (approximately ½ inch ribbon) into the conjunctival sac(s) four times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the post-operative period".

C. Basis for Approvability or Not-Approval Recommendation

During the review process, additional information was requested and the following critical quality issues were resolved:

- To evaluate the effect of temperature (40 and 50°C) on the dose uniformity of the ointment and on shipping stability, supporting studies were performed.
- For drug substance control, B&L will perform routine tests on reference standards.
- For drug product control, the acceptance criteria for Any Individual Unspecified Impurity in the drug product specification are tightened to NMT (b) (4)
- For proper drug release control, a test and acceptance criteria for "Particle Size Distribution" is included in the drug product specification.

For appropriate product quality control, a dose uniformity test and acceptance criteria was recommended to be included in the drug product specification for stability (FDA letters #4 dated Jun 25, 2010 and #5 dated Aug 12, 2010). Bausch & Lomb has developed an analytical procedure for dose uniformity and validated for use with the drug product for both the 3.5 gram and 1 gram fill size. The proposed testing procedure seems reasonable. However, the proposed acceptance criteria is not adequately justified with data.

A site recommendation of "Withhold" was made by the Office of Compliance for this application, since manufacturing facilities are not in compliance with current good manufacturing practice.

Therefore, this application is not recommended for approval until the following pending issues are resolved:

1. Satisfactory resolution of the inspectional deficiencies are required before this application may be approved.
2. Satisfactory responses to the following product quality deficiencies regarding the dose uniformity test are required before this application may be approved:
    a. Based on the summary information about the effect of storage time on dose uniformity which was provided in your amendment dated Sep 21, 2010, it is not possible to determine whether the proposed acceptance criteria are appropriate. Please submit the complete dataset from this study, so that the acceptance criteria can be established based on a more thorough analysis.
    b. Please also provide a risk assessment of an adverse impact on safety or efficacy at the dose uniformity ranges that are observed at longer storage times.

III. Administrative

A. Reviewer's Signature

_____ _____

Lin Qi, Ph.D. Date
Review Chemist

_____ _____

Stephen Miller, Ph.D. Date
Acting Branch Chief

B. Endorsement Block

ChemistName/Date: LQi/Sep 22, 2010
ChemistryBranchChiefName/Date: SMiller/Sep 22, 2010
ProjectManagerName/Date: FIzadi/Sep 22, 2010
ACuff/Sep 22, 2010
JDavid/Sep 22, 2010

C. CC Block: Listed in DARRTS

116 Page(s) have been Withheld in full as b4 (CCI/TS) immediately following this page

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/s/

LIN QI
09/30/2010

STEPHEN P MILLER
10/01/2010
I concur - from the CMC perspective NDA 200,738 cannot be approved until the deficiencies are resolved.

NDA FILEABILITY CHECKLIST

NDA Number: 200738
Applicant: Bausch & Lomb Incorporated
Letter Date: December 22, 2009
Stamp Date: December 22, 2009
Drug Name: Loteprednol Etabonate Ophthalmic Ointment, 0.5%

IS THE CMC SECTION OF THE APPLICATION FILEABLE? (Yes or No) __Yes__

The following parameters are necessary in order to initiate a full review, i.e., complete enough to review but may have deficiencies.

	Parameter	Yes	No	Comment
1	On its face, is the section organized adequately?	Y		
2	Is the section indexed and paginated adequately?	Y		This is an electronic submission
3	On its face, is the section legible?	Y		
4	Are ALL of the facilities (including contract facilities and test laboratories) identified with full street addresses and CFNs?	Y		
5	Is a statement provided that all facilities are ready for GMP inspection?	Y		
6	Has an environmental assessment report or categorical exclusion been provided?	Y		
7	Does the section contain controls for the drug substance?	Y		
8	Does the section contain controls for the drug product?	Y		
9	Has stability data and analysis been provided to support the requested expiration date?	Y		
10	Has all information requested during the IND phase, and at the pre-NDA meetings been included?	Y		Details to be reviewed
11	Have draft container labels been provided?	Y		
12	Has the draft package insert been provided?	Y		
13	Has an investigational formulations section been provided?	Y		
14	Is there a Methods Validation package?	Y		Columns to be shipped upon request
15	Is a separate microbiological section included?		N	

NDA 200738

Chemistry Reviewer: Lin Qi, Ph.D.
Pharmaceutical Assessment Lead: Linda Ng, Ph.D.
Acting Branch Chief: Stephen Miller, Ph.D.
Prepared by: LQ 1/26/10

DMF Number	Holder	Description	LOA Included	Status
(b) (4)		Loteprednol etabonate	Sep 3, 2009	
(b) (4)			Feb 5, 2008	

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-200738	ORIG-1	BAUSCH AND LOMB INC	LOTEPREDNOL ETABONATE OINTMENT, 0.5%

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/s/

LIN QI
01/25/2010

STEPHEN P MILLER
01/26/2010