CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 078208

Name: Naphazoline HCl 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution USP

Sponsor: Altaire Pharmaceuticals, Inc.

Approval Date: September 27, 2010

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 078208

Medvice Consulting, Inc.
U.S. Agent for: Altaire Pharmaceuticals, Inc.
Attention: Martin Dalsing
806 Kimball Avenue
Grand Junction, Colorado 81501

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated March 15, 2006 and accepted for filing on August 28, 2007, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Naphazoline Hydrochloride 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution, USP (OTC).

Reference is also made to your amendments dated June 26, 2006; August 27, 2007; September 9, and October 16, 2008; and January 13, February 2, February 3, February 20, March 3, and March 18, 2009; and March 15, 2010.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for over-the-counter (OTC) use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Naphazoline Hydrochloride 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution to be bioequivalent to the reference listed drug, Opcon-A® Ophthalmic Solution, (Naphazoline Hydrochloride 0.027% and Pheniramine Maleate 0.315%), of Bausch and Lomb, Inc.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical in content to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/U_CM072392.pdf

The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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

/s/

ROBERT L WEST

09/27/2010

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

LABELING

PLEASE READ CAREFULLY AND KEEP
THIS INSERT FOR FUTURE REFERENCE.

Naphazoline HCl 0.027% and
Pheniramine Maleate 0.315%
Ophthalmic Solution, USP

(With Antihistamine To Relieve Itching)

Itching & Redness Reliever Eye Drops
Eye Allergy Relief

- Temporarily relieves **itching and redness** caused by pollen, ragweed, grass, animal hair, and dander.
- Once available by prescription only, Naphazoline HCl 0.027% and Pheniramine Maleate 0.315%Ophthalmic Solution, USP is effective for the relief of itchy, red eyes.

INGREDIENTS: **(ACTIVE)** pheniramine maleate (0.315%), naphazoline hydrochloride (0.027%) (**INACTIVE**)benzalkonium chloride (0.01%), disodium edetate (0.1%), boric acid, hydroxypropyl methylcellulose, sodium borate, sodium chloride, purified water.

DIRECTIONS: **Adults and children 6 years of age and older:** Instill 1 or 2 drops in the affected eye(s) up to 4 times daily.
Children under 6 years: ask a doctor.

INDICATIONS: For the temporary relief of **redness and itching**of the eye due to pollen, ragweed, grass, animal hair and dander.

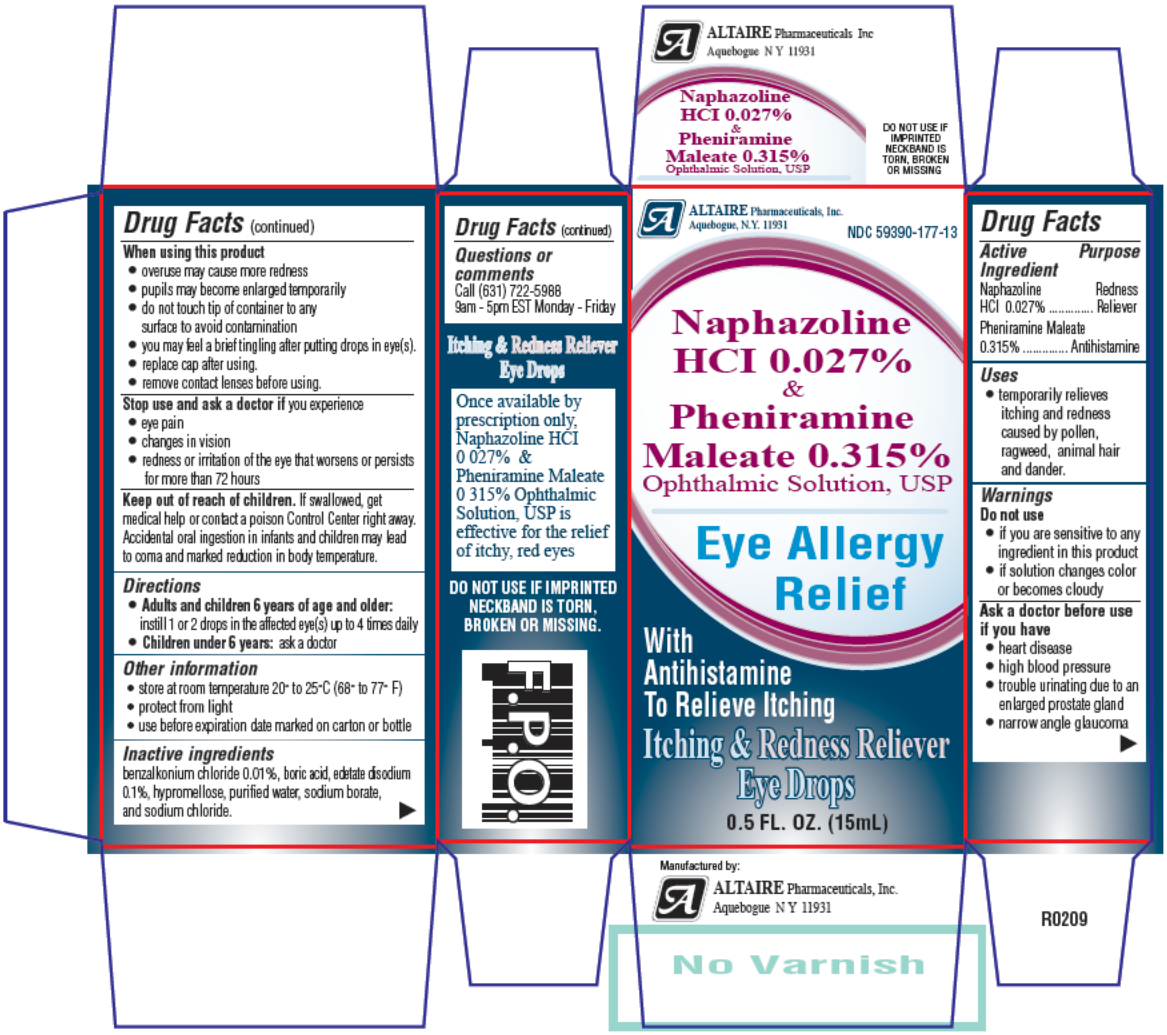
Front

WARNINGS:
If you are sensitive to any ingredient in this product, do not use.
To avoid contamination, do not touch tip of container to any surface. Replace cap after using. If solution changes color, or becomes cloudy, do not use.
Ask a doctor before use if you have • heart disease • high blood pressure • trouble urinating due to enlarged prostate gland • narrow angle glaucoma.
Stop use and ask a doctor if you experience: eye pain, changes in vision, redness or irritation of the eye that worsens or persists for more than 72 hours. Overuse of this product may produce increased redness of the eye. Pupils may become enlarged temporarily. You may experience a brief tingling sensation after putting drops in eyes.
Keep this and all drugs out of the reach of children. In case of accidental ingestion, seek professional assistance or contact a Poison Control Center immediately. Accidental oral ingestion in infants and children may lead to coma and marked reduction in body temperature.
Remove contact lenses before using.
Store at room temperature 20°-25°C(68°-77°F).
Protect from light.
Use before the expiration date marked on the carton or bottle.
Available in 15 mL NDC 59390-177-13 and 30 mL NDC 59390-177-18
Do not use if imprinted seal on cap is torn, broken or missing, or if imprinted seals on top and bottom flaps are not intact and completely legible.

Mfd By: ALTAIRE Pharmaceuticals, Inc.
Aquebogue N.Y. 11931

MG #18301 R0209

Back



- PMS

- PMS

- PMS

(b) (4)

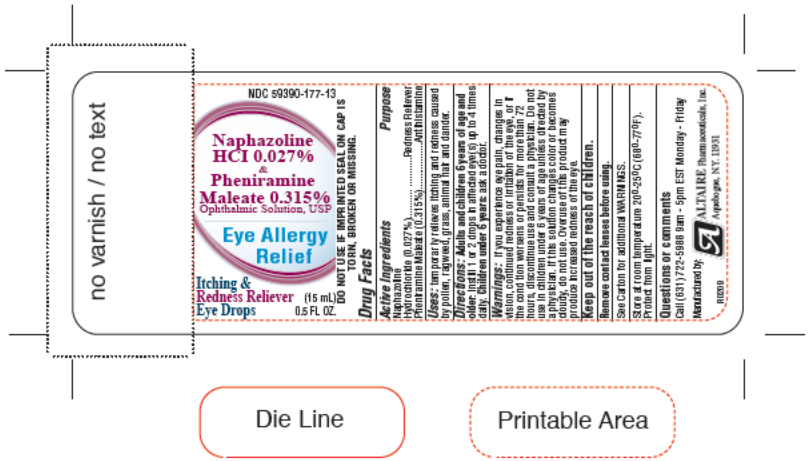
- PMS
- PMS
- PMS

(b) (4)

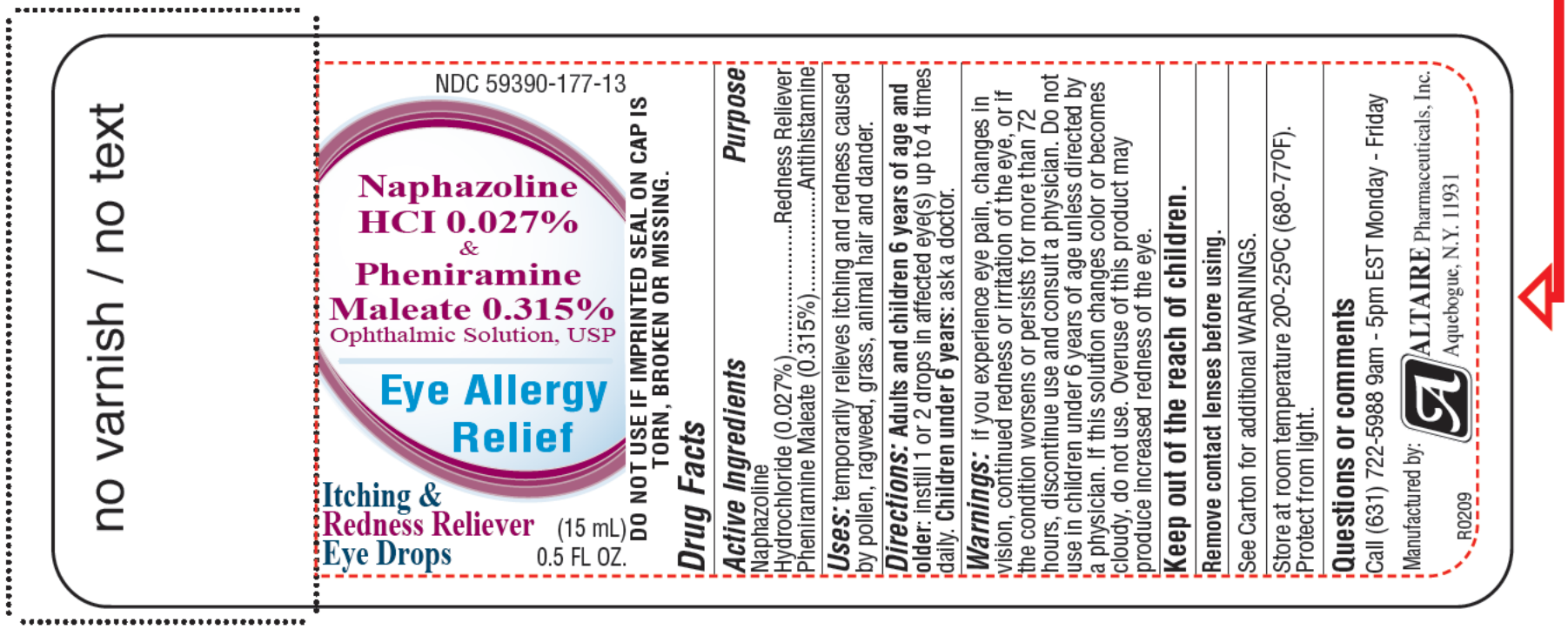
Naphazoline 1 fl oz Carton

Naphazoline 1/2 fl oz (15mL)
Boston round label

PROOF #: LABEL SIZE: **1.375" X 3.5"** PROOF SIZE (%): 100 DATE PROOF OUT: 2/19/09 PREPARED BY: (b) (6)	UPC CODE SPECS. MAGNIFICATION (%): B.W.A: -0.002"	COLORS CHECKED BY : _____ PLATES NEEDED .....> PMS .....> PMS (b) (4) This proof does not represent actual printed colors. Refer to PMS Book for actual color.



250 %



Naphazoline 1 fl oz (30 mL)
Boston round label

PROOF #: LABEL SIZE: **1.25" X 3.75"** PROOF SIZE (%): 100 DATE PROOF OUT: 2/19/09 PREPARED BY: (b) (6)	UPC CODE SPECS. MAGNIFICATION (%): B.W.A: -0.002"	COLORS PLATES NEEDED CHECKED BY : _____ .....> PMS_ (b) (4) .....> PMS_ This proof does not represent actual printed colors. Refer to PMS Book for actual color.

Die Line

Printable Area

250 %

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 78-208

Date of Submission: August 27, 2007

Applicant's Name: Altaire Pharmaceuticals, Inc.

Established Name: Naphazoline hydrochloride 0.027% and Pheniramine maleate 0.315% and ophthalmic solution, USP (OTC)

Labeling Deficiencies:

1. **GENERAL COMMENTS:**

   a. We have forwarded your proposed proprietary name, (b) (4) to the Division of Medication Errors and Technical Support (DMETS), for review and comment. We will inform you of their comments when they become available to us.

   b. Please note that your drug product is the subject of a USP monograph. We encourage you to include USP in the established name of your drug product.

2. **CONTAINER** (15 mL and 30 mL)

   a. **PRINCIPLE DISPLAY PANEL**: 21 CFR 201.61 (b) requires a statement of identity, **consisting of the established name of the drug** appearing on the principal display panel of an over-the-counter drug package. In addition, please note in that in accordance with 21 CRF 201.61 (c) the statement of identity shall be presented in bold face type on the principal display panel, and shall be in a size reasonably related to the most prominent printed matters on the principle display panel. Revise to include the established names and concentrations of the active ingredients **"naphazoline hydrochloride 0.027% and pherniramine maleate 0.315% ophthalmic solution, USP"** following your proposed proprietary name.

   b. Revise your storage temperature to read as "store at 20°-25°C (68°-77°F)".

   c. In order for us to verify your compliance with the labeling format requirements of 21 CFR 201.66 (Format and content of OTC labeling), please submit a format legend for each size of your labels.

   d. Bold the pharmacological category **"Itching and Redness Reliever Eye Drops".** Refer to 21 CRF 201.61 (c) for further guidance.

   e. Inactive ingredients: Revise (b) (4) to read as "purified water" to be consistent with your "components and composition" statement.

   f. Delete (b) (4)

   g. It is difficult to read the information on your container label. Please note that it is not necessary to have all the required information for an OTC product placed on your container label when there is an outside container (carton) provided with all the required information. Refer to 21 CRF 201.66 (c) for further guidance. Please revise you container label to be the same as the reference listed drug, Opcon-A (NDA 20-065/S-017: Approved July 31, 2007). We refer you to http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

3. **CARTON:** (15 mL and 30 mL)

   a. See **CONTAINER** COMMENTS (a) through (e).

   b. **Side Panel and Back Panel-Top Flap** – Include the established names and concentrations of the active ingredients, **naphazoline hydrochloride 0.027% and pheniramine maleate 0.315% ophthalmic solution, USP** following your proposed proprietary name.

   c. **PRINCIPAL DISPLAY PANEL**: Delete "Available without a prescription" as this information appears on the side panel.

   d. Add the statement "With antihistamine to relieve itching" as does the reference listed drug.

4. **PATIENT INFORMATION SHEET:**

   a. Include the established names and concentrations of the active ingredients, **naphazoline hydrochloride 0.027% and pheniramine maleate 0.315% ophthalmic solution, USP** following your proposed proprietary name.

   b. See Container comment (b) and (e).

Revise your labeling, as instructed above, and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission, please provide a side-by-side comparison of your proposed labeling with that of your last submission with all differences annotated and explained.

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have Final Printed Labels and Labeling?

- **Container Labels**: (15 mL) - Satisfactory in FPL as of
- **Carton Labeling:** (15 mL) – Satisfactory in FPL as of
- **Container Labels**: (30 mL) - Satisfactory in FPL as of
- **Carton Labeling:** (30 mL) – Satisfactory in FPL as of

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Opcon-A
- NDA Number: 20-065
- NDA Drug Name: naphazoline hydrochloride 0.027% and pheniramine maleate 0.315% ophthalmic solution, USP
- NDA Firm: Bausch and Lomb
- Date of Approval of NDA Insert: NDA 20-065/S-017: Approved July 31, 2007
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labels: Side-by-side comparison
- Revisions needed post-approval:
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 20-065

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.		none

Exclusivity Data– NDA 20-065

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

NOTE TO CHEMIST:

FOR THE RECORD:

1. **MODELING LABELING:** Labeling review based on the reference listed drug Opcon-A (NDA 20-065/S-017: Approved July 31, 2007.

CARTON: Please note that the RLD use to have a statement “Once available by prescription only, Opcon is effective for the relief of itchy red eyes” on their carton. The RLD deleted this statement due to space constraints and replaced it with “original prescription strength”. The generic firm included the former RLD statement on their carton labeling. Since this statement was deleted by the firm for space constraints and the agency did not ask for removal, the generic firm will be allow to have that statement on their carton labeling.

ESTABLISHED NAME: Please note hat the RLD labels and labeling have the order of the active ingredients for the established name listed as pheniramine maleate and naphazoline hydrochloride rather than Naphazoline hydrochloride and Pheniramine maleate ophthalmic solution, USP. The established name for this product based on the orange book and USP monograph is Naphazoline hydrochloride and Pheniramine maleate ophthalmic solution, USP. The firm was asked to follow the orange book/USP monograph for the listing of the order of the active ingredients for the established name of this drug product.

2. **INACTIVE INGREDIENTS;** The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components.

Ingredient	Quantity per mL	THEORETICAL Quantity per ANDA Bach (b) (4)	Pharmaceutical Function
Naphazoline hydrochloride, USP	0.2675 mg	(b) (4)	Active ingredient
Pheniramine maleate, USP	3.1500 mg		Active ingredient
Hydroxypropyl methylcellulose, USP	(b) (4)		(b) (4)
Purified water, USP	q.s. to 1 ml		
Boric acid, NF	(b) (4)		
Sodium borate, NF			
Sodium chloride, USP			
(b) (4)			
Edetate disodium, USP	1.0000 mg		
Benzalkonium chloride, USP	0.1000 mg		
(b) (4)			

Description: Clear, colorless solution
The firm has provided a satisfactory comparison of the unit and ANDA batch composition.

3. **PATENTS/EXCLUSIVITIES**

Patent Data – NDA 20-065

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.		none

Exclusivity Data– NDA 20-065

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

4. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON USP:**

- **USP:** Preserve in tight containers, and store at a temperature between 20° and 25°, protected from light.
- **RLD:** "Stored at 20° - 25°C (68° - 77°F) Protect from light.
- **ANDA:** Store at (b) (4) Protect from light

5. **PACKAGING CONFIGURATIONS**

RLD: 15 mL bottle
ANDA: Packaging configuration and sizes: 15cc and 30cc bottles, tips and caps.

6. **CONTAINER/CLOSURE**

Bottle, 15cc: Low Density Polyethylene (b) (4) **Round 15mm neck**
Tamper Evident Bead
Resin: (b) (4) LDPE (b) (4)
Color: (b) (4) White

Bottle, 30cc: Low Density Polyethylene [redacted] **Round 15mm neck**
Tamper Evident Bead
Resin: [redacted] LDPE [redacted]
Color: [redacted] White

Low Density Polyethylene 15 mm Dropper-controlled Dropper
Tip 0.02 Needle
Resin: [redacted]
Color: Natural
Dropper Tip Cap: Polypropylene [redacted] Dropper Tip Cap
Resin: [redacted]
Color: White [redacted]

7. FINISHED DOSAGE FORM:
NDA: Clear, colorless solution

ANDA: Clear, colorless solution

8. FINISHED DOSAGE MANUFACTURING FACILITY
Altaire Pharmaceuticals, Inc.,
311 West Lane
PO Box 849
Aquebogue, NY 11931

Date of Submission: August 27, 2007

Primary Reviewer: B. Weitzman **Date:**

Team Leader: John Grace **Date:**

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

/s/

Beverly Weitzman
8/5/2008 07:56:30 PM
LABELING REVIEWER

John Grace
8/6/2008 12:01:47 PM
LABELING REVIEWER

APPROVAL SUMMARY #1
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 78-208

Date of Submission: February 20, 2009

Applicant's Name: Altaire Pharmaceuticals, Inc.

Established Name: Naphazoline hydrochloride 0.027% and Pheniramine maleate 0.315% and ophthalmic solution, USP (OTC)

APPROVAL SUMMARY (List the package size, strength(s), and date of submission for approval):
Do you have Final Printed Labels and Labeling? YES

- **Container Labels**: (15 mL) - Satisfactory in FPL as of **February 20, 2009** electronic submission**.**

\\Fdswa150\nonectd\N78208\N_000\2009-02-20\Naphazoline_PDFs\15_mL_Naphazoline(PDF)\Naphazoline_(05ozLabel).pdf

- **Carton Labeling:** (15 mL) – Satisfactory in FPL as of **February 20, 2009** electronic submission**.**

\\Fdswa150\nonectd\N78208\N_000\2009-02-20\Naphazoline_PDFs\15_mL_Naphazoline(PDF)\Naphazoline_(05ozCarton).pdf

Container Labels: (30 mL) - Satisfactory in FPL as of **February 20, 2009** electronic submission**.**
\\Fdswa150\nonectd\N78208\N_000\2009-02-20\Naphazoline_PDFs\30_mL_Naphazoline(PDF)\Naphazoline_(1ozLabel).pdf

- **Carton Labeling:** (30 mL) – Satisfactory in FPL as of **February 20, 2009** electronic submission**.**

\\Fdswa150\nonectd\N78208\N_000\2009-02-20\Naphazoline_PDFs\30_mL_Naphazoline(PDF)\Naphazoline_(1ozCarton).pdf

- **Patient Information Sheet:** Satisfactory in FPL as of **February 20, 2009** electronic submission**.**

\\Fdswa150\nonectd\N78208\N_000\2009-02-20\Naphazoline_PDFs\Naphazoline_insert(PDF)\insert_Naphazoline.pdf

BASIS OF APPROVAL:

- Was this approval based upon a petition? No
- What is the RLD on the 356(h) form: Opcon-A
- NDA Number: 20-065
- NDA Drug Name: naphazoline hydrochloride 0.027% and pheniramine maleate 0.315% ophthalmic solution, USP
- NDA Firm: Bausch and Lomb
- Date of Approval of NDA Insert: NDA 20-065/S-017: Approved July 31, 2007
- Has this been verified by the MIS system for the NDA? Yes
- Was this approval based upon an OGD labeling guidance? No
- Basis of Approval for the Container Labels: Side-by-side comparison
- Basis of Approval for the Carton Labels: Side-by-side comparison
- Revisions needed post-approval:
- Patents/Exclusivities: Refer to chart below.

Patent Data – NDA 20-065

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.		none

Exclusivity Data– NDA 20-065

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

NOTE TO CHEMIST:

FOR THE RECORD:

1. **MODELING LABELING:** Labeling review based on the reference listed drug Opcon-A (NDA 20-065/S-017: Approved July 31, 2007.

CARTON: Please note that the RLD use to have a statement "Once available by prescription only, Opcon is effective for the relief of itchy red eyes" on their carton. The RLD deleted this statement due to space constraints and replaced it with "original prescription strength". The generic firm included the former RLD statement on their carton labeling. Since this statement was deleted by the firm for space constraints and the agency did not ask for removal, the generic firm will be allow to have that statement on their carton labeling.

ESTABLISHED NAME: Please note hat the RLD labels and labeling have the order of the active ingredients for the established name listed as pheniramine maleate and naphazoline hydrochloride rather than Naphazoline hydrochloride and Pheniramine maleate ophthalmic solution, USP. The established name for this product based on the orange book and USP monograph is Naphazoline hydrochloride and Pheniramine maleate ophthalmic solution, USP. The firm was asked to follow the orange book/USP monograph for the listing of the order of the active ingredients for the established name of this drug product.

2. **PROPOSED PROPRIETARY:** (b) (4) (Naphazoline Hydrochloride and Pheniramine Maleate) Ophthalmic Solution 0.02675 % / 0.315 %: **The name was found unacceptable**

PORTION of NAME CONSULT: The Proprietary Name Risk Assessment findings indicate that (b) (4)

As such, the Medication Error Staff objects to the use of the proprietary name (b) (4) **for this product.**

3. **INACTIVE INGREDIENTS;** The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the statement of components.

Ingredient	Quantity per mL	THEORETICAL Quantity per ANDA Bach (b) (4)	Pharmaceutical Function
Naphazoline hydrochloride, USP	0.2675 mg	(b) (4)	Active ingredient
Pheniramine maleate, USP	3.1500 mg		Active ingredient
Hydroxypropyl methylcellulose, USP	(b) (4)		(b) (4)
Purified water, USP	q.s. to 1 ml		
Boric acid, NF	(b) (4)		
Sodium borate, NF			
Sodium chloride, USP			
(b) (4)			
Edetate disodium, USP	1.0000 mg		
Benzalkonium chloride, USP	0.1000 mg		
(b) (4)			

Description: Clear, colorless solution

The firm has provided a satisfactory comparison of the unit and ANDA batch composition.

4. **PATENTS/EXCLUSIVITIES**

Patent Data – NDA 20-065

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
			There are no unexpired patents for this product in the Orange Book Database.		none

Exclusivity Data– NDA 20-065

Code	Reference	Expiration	Labeling Impact
NONE	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	NONE

5. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON USP:**

- **USP:** Preserve in tight containers, and store at a temperature between 20° and 25°, protected from light.
- **RLD:** "Stored at 20° - 25°C (68° - 77°F) Protect from light.
- **ANDA:** Store at (b) (4) Protect from light

6. **PACKAGING CONFIGURATIONS**

RLD: 15 mL bottle

ANDA: Packaging configuration and sizes: 15cc and 30cc bottles, tips and caps.

7 **CONTAINER/CLOSURE**

Bottle, 15cc: Low Density Polyethylene (b) (4) Round 15mm neck
Tamper Evident Bead
Resin: (b) (4) LDPE (b) (4)
Color: (b) (4) White

Bottle, 30cc: Low Density Polyethylene (b) (4) Round 15mm neck
Tamper Evident Bead
Resin: (b) (4) LDPE (b) (4)
Color: White

Low Density Polyethylene 15 mm Dropper-controlled Dropper
Tip 0.02 Needle
Resin: (b) (4)
Color: Natural
Dropper Tip Cap: Polypropylene (b) (4) Dropper Tip Cap
Resin: (b) (4)
Color: White (b) (4)

8. FINISHED DOSAGE FORM:
NDA: Clear, colorless solution

ANDA: Clear, colorless solution

9. FINISHED DOSAGE MANUFACTURING FACILITY
Altaire Pharmaceuticals, Inc.,
311 West Lane
PO Box 849
Aquebogue, NY 11931

Date of Submission: February 20, 2009

Primary Reviewer: B. Weitzman **Date:**

Team Leader: John Grace **Date:**

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

/s/

Beverly Weitzman
3/17/2009 09:46:59 AM
LABELING REVIEWER

John Grace
3/17/2009 10:31:45 AM
LABELING REVIEWER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

CHEMISTRY REVIEWS

ANDA 78-208

Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution, 0.027% and 0.315%

Altaire Pharmaceuticals

Mahnaz Farahani, Ph.D.
Division of Chemistry I
Office of Generic Drugs

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-208 First Generic

2. REVIEW #: 1

3. REVIEW DATE: 12/30/07

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
N/A	N/A

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original submission	3/15/06
Amendment	6/26/06
General correspondence	5/6 and 8/27/07
Acceptable for filing	8/28/07

7. NAME & ADDRESS OF APPLICANT:

Name:	Altaire Pharmaceuticals, Inc.
Address:	PO Box 849 311 West Lane Aquebogue, NY 11931
Representative:	Medvice Consulting, Inc. 2214 Sanford Drive, Suite B7 Grand Junction, CO 81505
Telephone:	970-243-5490

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: (b) (4)
b) Non-Proprietary Name (USAN): Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided Paragraph II Patent Certification Statement.

The reference listed drug is Opcon-A®, manufactured by Bausch and Lomb, NDA 20-065.

10. PHARMACOL CATEGORY:

Temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

11. DOSAGE FORM:

Ophthalmic Solution

12. STRENGTH/POTENCY:

Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

13. ROUTE OF ADMINISTRATION:

Topical

14. Rx/OTC DISPENSED: ___Rx __x_OTC

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

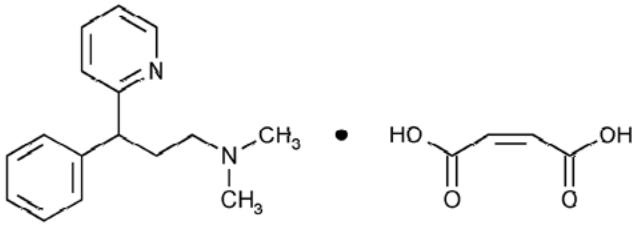
_____SPOTS product – Form Completed

__x____Not a SPOTS product

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

Pheniramine Maleate

Chemistry Review Data Sheet

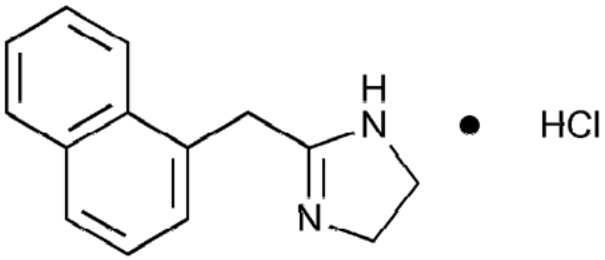


$C_{16}H_{20}N_2 \cdot C_4H_4O_4$ 356.42

2-[α-[2-Dimethylaminoethyl]benzyl]pyridine bimaleate.

N,*N*-Dimethyl-3-phenyl-3-(2-pyridyl)propylamine hydrogen maleate

Naphazoline Hydrochloride



$C_{14}H_{14}N_2 \cdot HCl$ 246.74

1*H*-Imidazole, 4,5-dihydro-2-(1-naphthalenylmethyl)-, monohydrochloride.

2-(1-Naphthylmethyl)-2-imidazoline monohydrochloride

17. RELATED/SUPPORTING DOCUMENTS:

Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Inadequate	12/30/07	M Farahani
	II			1	Inadequate	2/4/08	M Farahani
	III			4			
	III			4			

[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: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	**RECOMMENDATION**	**DATE**	**REVIEWER**
Microbiology	Pending		
EES	Pending		
Methods Validation	Not required		
Labeling	Pending		
Bioequivalence	Pending		
EA	Categorical exclusion	3/6/06	M. Farahani
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. _x___ Yes _____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 78-208

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is not approvable due to minor deficiencies.

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)

Drug Substance:

Naphazoline Hydrochloride, USP manufactured by:
(b) (4)

Naphazoline Hydrochloride, USP is White to off-white crystalline powder. The pH is 5.0-6.6 and solution is clear and colorless. It is soluble in water.

DMF (b) (4) describes the synthesis of the drug substance Naphazoline Hydrochloride, USP. The DMF was reviewed by M. Farahani on February 4, 2008 and was found to be inadequate.

Pheniramine Maleate, USP manufactured by:
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Pheniramine Maleate, USP is a white fine crystalline powder. The melting point is 104°C-109°C.

DMF (b) (4) describes the synthesis of the drug substance Pheniramine Maleate, USP. The DMF was reviewed by M. Farahani on December 30, 2007 and was found to be inadequate.

Drug product: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%. Ophthalmic Solution temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

Inactive ingredients in the formulation are: Hydroxypropyl methylcellulose, USP, Purified water, USP, Boric acid, NF, Sodium borate, NF, Sodium chloride, USP, Edetate disodium, USP, Benzalkonium chloride, USP, (b) (4) (b) (4).

An expiration date of 24 months has been requested based on 3-months of accelerated stability data. In addition to the accelerated stability data, the firm has also submitted 24 months of room temperature stability data. The stability data support the requested expiration date of 24 months.

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

The recommended storage condition is [redacted] (b) (4). Protect from light.
The drug product is an ophthalmic solution. The labeling insert states to apply 1-2 drops in each affected eye up to four times daily. 1 drop ≈ 50 mg (USP).

Naphazoline HCl 0.027%:
MDD=50 mg x 8 drops x 2 eyes x 0.027%= 0.216 mg/day
DS: IT= 0.10% QT= 0.15%
DP: IT = 1.0% QT = 1.0%

Pheniramine Maleate 0.315%:
MDD=50 mg x 8 drops x 2 eyes x 0.315%= 2.52 mg/day
DS: IT= 0.10% QT= 0.15%
DP: IT = 0.50% QT = 1.0%

C. Basis for Approvability or Not-Approval Recommendation

This application is not approvable due to minor deficiencies.

III. Administrative

A. Reviewer's Signature

Mahnaz Farahani, Ph.D.

B. Endorsement Block

James M. Fan

Following this page, 10 pages withheld in full (b)(4)

(b) (4)

30. MICROBIOLOGY: Pending

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS: Not required

32. LABELING: Pending

33. ESTABLISHMENT INSPECTION : Pending

34. BIOEQUIVALENCE: Pending

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: Satisfactory

The firm requests a waiver of the Environmental Assessment in accordance with 21 CFR 25.31 (a).

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78- 208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Drug Master File (DMF) No. (b) (4) has been found deficient. The DMF holder has been informed of the deficiencies. Please do not respond to this letter until you have received notification from the DMF holder that all deficiencies have been addressed, and a DMF amendment has been submitted to the Agency.

2. Drug Master File (DMF) No. (b) (4) has been found deficient. The DMF holder has been informed of the deficiencies. Please do not respond to this letter until you have received notification from the DMF holder that all deficiencies have been addressed, and a DMF amendment has been submitted to the Agency.

3. Please provide (b) (4)

4. The specification for (b) (4) .

5. We note you have provided (b) (4)

6. Please submit [redacted] (b) (4)

7. Please include [redacted] (b) (4)

8. Please submit [redacted] (b) (4)

9. Please submit [redacted] (b) (4)

10. Please provide [redacted] (b) (4)

11. Please clarify [redacted] (b) (4)

12. Please include [redacted] (b) (4)

13. Please include [redacted] (b) (4)

14. Please include [redacted] (b) (4)

15. Please provide [redacted] (b) (4)

16. We notice tha [redacted] (b) (4)

17. Please conduct [redacted] (b) (4)

18. Please revise [redacted] (b) (4)

[redacted] (b) (4)

19. Please include [redacted] (b) (4).

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of approval.

2. Bioequivalence, Microbiology and Labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under a separate cover.

3. Please conduct your future drug product accelerated stability testing at (40 ºC +/-2 ºC/ 25% RH± 5%RH).

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 78- 208
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-624/M.Farahani/12/30/07
HFD-627/J.Fan/
HFD-617/R.Adigun

F/T:

V:\Chemistry Division I\Team 3\FIRMSAM\Altaire\78208.R01.doc

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

/s/

Mahnaz Farahani
2/14/2008 11:28:50 AM
CHEMIST

Rosalyn Adigun
2/29/2008 02:11:31 PM
CSO

James Fan
3/3/2008 12:51:04 PM
CHEMIST

ANDA 78-208

Pheniramine Maleate and Naphazoline Hydrochloride Ophthalmic Solution, 0.315% and 0.027%

Altaire Pharmaceuticals, Inc.

Mahnaz Farahani, Ph.D.
Division of Chemistry I
Office of Generic Drugs

Review # 2

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-208 First Generic

2. REVIEW #: 2

3. REVIEW DATE: July 22, 2008

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original submission	3/15/06
Amendment	6/26/06
General correspondence	5/6 and 8/27/07
Acceptable for filing	8/28/07

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	May 21, 2008

7. NAME & ADDRESS OF APPLICANT:

Name:	Altaire Pharmaceuticals, Inc.
Address:	PO Box 849 311 West Lane Aquebogue, NY 11931
Representative:	Medvice Consulting, Inc. 2214 Sanford Drive, Suite B7 Grand Junction, CO 81505
Telephone:	970-243-5490

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: (b) (4)

b) Non-Proprietary Name (USAN): Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided Paragraph II Patent Certification Statement.

The reference listed drug is Opcon-A®, manufactured by Bausch and Lomb, NDA 20-065.

10. PHARMACOL CATEGORY:

Temporally relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

11. DOSAGE FORM:

Ophthalmic Solution

12. STRENGTH/POTENCY:

Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

13. ROUTE OF ADMINISTRATION:

Topical

14. Rx/OTC DISPENSED: ___Rx __x_OTC

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

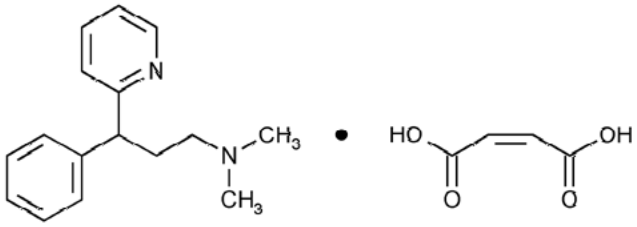
_____SPOTS product – Form Completed

__x____Not a SPOTS product

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

Pheniramine Maleate

Chemistry Review Data Sheet

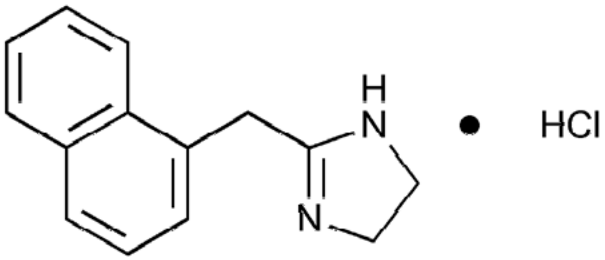


$C_{16}H_{20}N_2 \cdot C_4H_4O_4$ 356.42

2-[α-[2-Dimethylaminoethyl]benzyl]pyridine bimaleate.

N,*N*-Dimethyl-3-phenyl-3-(2-pyridyl)propylamine hydrogen maleate

Naphazoline Hydrochloride



$C_{14}H_{14}N_2 \cdot HCl$ 246.74

1*H*-Imidazole, 4,5-dihydro-2-(1-naphthalenylmethyl)-, monohydrochloride.

2-(1-Naphthylmethyl)-2-imidazoline monohydrochloride

17. RELATED/SUPPORTING DOCUMENTS:

Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Adequate	7/21/08	M Farahani
	II			1	Adequate	7/22/08	M Farahani
	III			4			
	III			4			

[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: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	**RECOMMENDATION**	**DATE**	**REVIEWER**
Microbiology	Pending		
EES	Pending		
Methods Validation	Not required		
Labeling	Pending		
Bioequivalence	Pending		
EA	Categorical exclusion	3/6/06	M. Farahani

Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes ___x_ No If no, explain reason(s) below: Minor amendment

The Chemistry Review for ANDA 78-208

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is not acceptable.

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)

Drug Substance:

Naphazoline Hydrochloride, USP manufactured by:
(b) (4)

Naphazoline Hydrochloride, USP is White to off-white crystalline powder. The pH is 5.0-6.6 and solution is clear and colorless. It is soluble in water.

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Pheniramine Maleate, USP is a white fine crystalline powder. The melting point is 104°C-109°C.

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Drug product: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%. Ophthalmic Solution temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

Inactive ingredients in the formulation are: Hydroxypropyl methylcellulose, USP, Purified water, USP, Boric acid, NF, Sodium borate, NF, Sodium chloride, USP, Edetate disodium, USP, Benzalkonium chloride, USP, (b) (4) .

An expiration date of 24 months has been requested based on 3-months of accelerated stability data. In addition to the accelerated stability data, the firm has also submitted 24 months of room temperature stability data. The stability data support the requested expiration date of 24 months.

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

The recommended storage condition is 15º – 30ºC (59º – 86ºF). Protect from light.
The drug product is an ophthalmic solution. The labeling insert states to apply 1-2 drops in each affected eye up to four times daily. 1 drop ≈ 50 mg (USP).

Naphazoline HCl 0.027%:
MDD=50 mg x 8 drops x 2 eyes x 0.027%= 0.216 mg/day
DS: IT= 0.10% QT= 0.15%
DP: IT = 1.0% QT = 1.0%

Pheniramine Maleate 0.315%:
MDD=50 mg x 8 drops x 2 eyes x 0.315%= 2.52 mg/day
DS: IT= 0.10% QT= 0.15%
DP: IT = 0.50% QT = 1.0%

C. Basis for Approvability or Not-Approval Recommendation

The application is not acceptable

III. Administrative

A. Reviewer's Signature

Mahnaz Farahani, Ph.D.

B. Endorsement Block

James M. Fan

Following this page, 17 pages withheld in full (b)(4)

Response: All future stability testing for the subject drug product shall be conducted on sampled held under accelerated conditions of (40 ºC +2 ºC/ 25% RH± 5%RH).

30. MICROBIOLOGY: Pending

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS: Not required

32. LABELING: Pending

33. ESTABLISHMENT INSPECTION : Pending

34. BIOEQUIVALENCE: Pending

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: Satisfactory

The firm requests a waiver of the Environmental Assessment in accordance with 21 CFR 25.31 (a).

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78- 208 APPLICANT: Altaire Pharmaceuticals, Inc.

DRUG PRODUCT: Pheniramine Maleate 0.315% and Naphazoline Hydrochloride 0.027% Ophthalmic Solution

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please provide (b) (4) .
2. Please provide (b) (4) .
3. Please provide (b) (4)
4. Please provide (b) (4) .
5. Please provide (b) (4)
6. The validation of (b) (4) .
7. Please provide (b) (4)
8. Please provide (b) (4)

9. Please provide [redacted] (b) (4)

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of approval.

2. Bioequivalence, Microbiology and Labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under a separate cover.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 78- 208
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-624/M.Farahani/7/22/08
HFD-627/J.Fan/
HFD-617/R.Adigun

F/T:

V:\Chem I\Team 3\FIRMSAM\ Altaire \LTRS&REV\78208.R02.doc

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

/s/

Mahnaz Farahani
8/20/2008 10:47:01 AM
CHEMIST

Simon Eng
8/20/2008 11:21:17 AM
CSO

James Fan
8/21/2008 08:35:01 AM
CHEMIST

ANDA 78-208

Pheniramine Maleate and Naphazoline Hydrochloride Ophthalmic Solution, 0.315% and 0.027%

Altaire Pharmaceuticals, Inc.

Mahnaz Farahani, Ph.D.
Division of Chemistry I
Office of Generic Drugs

Review # 3

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-208 First Generic

2. REVIEW #: 3

3. REVIEW DATE: September 16, 2009

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original submission	3/15/06
Amendment	6/26/06
General correspondence	5/6 and 8/27/07
Acceptable for filing	8/28/07
Amendment	May 21, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	September 9, 2008

7. NAME & ADDRESS OF APPLICANT:

Name:	Altaire Pharmaceuticals, Inc.
Address:	PO Box 849 311 West Lane Aquebogue, NY 11931
Representative:	Medvice Consulting, Inc. 2214 Sanford Drive, Suite B7 Grand Junction, CO 81505
Telephone:	970-243-5490

8. DRUG PRODUCT NAME/CODE/TYPE:

Chemistry Review Data Sheet

a) Proprietary Name: (b) (4)
b) Non-Proprietary Name (USAN): Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided Paragraph II Patent Certification Statement.

The reference listed drug is Opcon-A®, manufactured by Bausch and Lomb, NDA 20-065.

10. PHARMACOL CATEGORY:

Temporally relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

11. DOSAGE FORM:

Ophthalmic Solution

12. STRENGTH/POTENCY:

Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

13. ROUTE OF ADMINISTRATION:

Topical

14. Rx/OTC DISPENSED: ___Rx __x_OTC

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

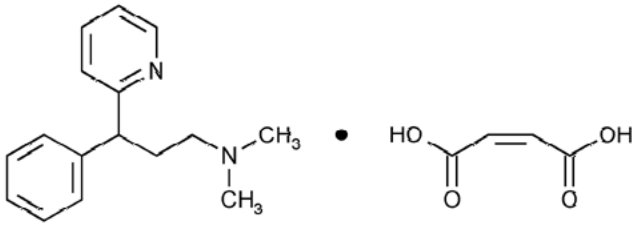
_____SPOTS product – Form Completed

__x____Not a SPOTS product

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

Pheniramine Maleate

Chemistry Review Data Sheet

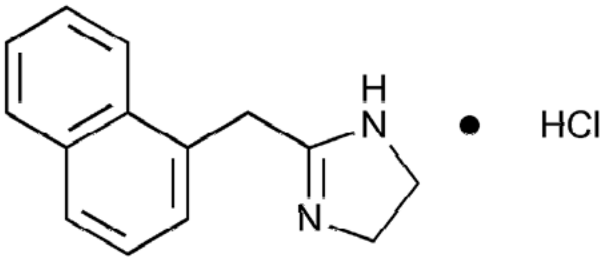


$C_{16}H_{20}N_2 \cdot C_4H_4O_4$ 356.42

2-[α-[2-Dimethylaminoethyl]benzyl]pyridine bimaleate.

N,*N*-Dimethyl-3-phenyl-3-(2-pyridyl)propylamine hydrogen maleate

Naphazoline Hydrochloride



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2-(1-Naphthylmethyl)-2-imidazoline monohydrochloride

17. RELATED/SUPPORTING DOCUMENTS:

Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
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	III			4			

[1] Action codes for DMF Table:
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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: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	Acceptable	5/1/09	Steven Donald
EES	Pending (please see Approval Routing Summary for final recommendation)		
Methods Validation	Not required		
Labeling	Acceptable	3/17/09	Beverly Weitzman
Bioequivalence	Acceptable	3/16/09	Farrar, Johnetta L

EA	Categorical exclusion	3/6/06	M. Farahani
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes ___x_ No If no, explain reason(s) below: Minor amendment

The Chemistry Review for ANDA 78-208

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is approvable.

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

N/A

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MDD=50 mg x 8 drops x 2 eyes x 0.027%= 0.216 mg/day
DS: IT= 0.10% QT= 0.15%
DP: IT = 1.0% QT = 1.0%

Pheniramine Maleate 0.315%:
MDD=50 mg x 8 drops x 2 eyes x 0.315%= 2.52 mg/day
DS: IT= 0.10% QT= 0.15%
DP: IT = 0.50% QT = 1.0%

C. Basis for Approvability or Not-Approval Recommendation

The application is approvable.

III. Administrative

A. Reviewer's Signature

Mahnaz Farahani, Ph.D.

B. Endorsement Block

James M. Fan/ TL

Following this page, 10 pages withheld in full (b)(4)

30. MICROBIOLOGY: Acceptable 5/1/09 (S. Donald)

31. SAMPLES AND RESULTS/METHODS VALIDATION STATUS: Not required

32. LABELING: Acceptable 3/17/09 (B. Weitzman)

33. ESTABLISHMENT INSPECTION : Pending

34. BIOEQUIVALENCE: Acceptable 3/16/09 (J Farrar)

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION: Satisfactory

The firm requests a waiver of the Environmental Assessment in accordance with 21 CFR 25.31 (a).

cc: ANDA 78- 208
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-624/M.Farahani/1/05/10
HFD-627/J.Fan/1/5/10
HFD-617/T. Tran/1/6/10

F/T:

V:\Chem I\Team 3\FIRMSAM\ Altaire \LTRS&REV\78208.R03.doc

TYPE OF LETTER: CMC is approvable

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-78208	ORIG-1	ALTAIRE PHARMACEUTICALS INC	NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE

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

/s/

MAHNAZ FARAHANI
01/11/2010

JAMES M FAN
01/11/2010

TRANG Q TRAN
01/11/2010

ANDA 78-208

Pheniramine Maleate and Naphazoline Hydrochloride Ophthalmic Solution, 0.315% and 0.027%

Altaire Pharmaceuticals, Inc.

Mahnaz Farahani, Ph.D.
Division of Chemistry I
Office of Generic Drugs

Review # 4

Table of Contents

Chemistry Review Data Sheet

1. ANDA: 78-208 First Generic

2. REVIEW #: 4

3. REVIEW DATE: September 1, 2010

4. REVIEWER: Mahnaz Farahani, Ph.D.

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original submission	3/15/06
Amendment	6/26/06
General correspondence	5/6 and 8/27/07
Acceptable for filing	8/28/07
Amendment	May 21, 2008
Amendment	September 9, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	March 15, 2010

7. NAME & ADDRESS OF APPLICANT:

Name:	Altaire Pharmaceuticals, Inc.
Address:	PO Box 849 311 West Lane Aquebogue, NY 11931
Representative:	Medvice Consulting, Inc. 2214 Sanford Drive, Suite B7 Grand Junction, CO 81505
Telephone:	970-243-5490

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: (b) (4)
b) Non-Proprietary Name (USAN): Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

9. LEGAL BASIS FOR SUBMISSION:

The firm has provided Paragraph II Patent Certification Statement.

The reference listed drug is Opcon-A®, manufactured by Bausch and Lomb, NDA 20-065.

10. PHARMACOL CATEGORY:

Temporally relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

11. DOSAGE FORM:

Ophthalmic Solution

12. STRENGTH/POTENCY:

Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

13. ROUTE OF ADMINISTRATION:

Topical

14. Rx/OTC DISPENSED: ___Rx __x_OTC

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

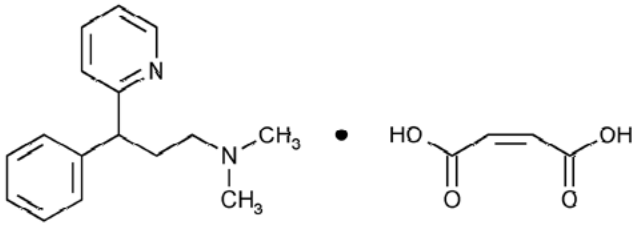
_____SPOTS product – Form Completed

__x____Not a SPOTS product

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

Pheniramine Maleate

Chemistry Review Data Sheet

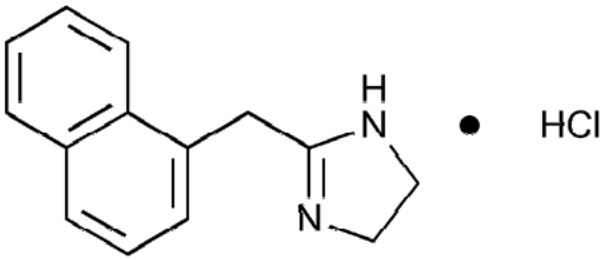


$C_{16}H_{20}N_2 \cdot C_4H_4O_4$ 356.42

2-[α-[2-Dimethylaminoethyl]benzyl]pyridine bimaleate.

N,*N*-Dimethyl-3-phenyl-3-(2-pyridyl)propylamine hydrogen maleate

Naphazoline Hydrochloride



$C_{14}H_{14}N_2 \cdot HCl$ 246.74

1*H*-Imidazole, 4,5-dihydro-2-(1-naphthalenylmethyl)-, monohydrochloride.

2-(1-Naphthylmethyl)-2-imidazoline monohydrochloride

17. RELATED/SUPPORTING DOCUMENTS:

Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)	II		(b) (4)	1	Adequate	9/19/10	Reviewed by M Farahani
	II			1	Adequate	9/19/10	M Farahani
	III			4			
	III			4			

[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: N/A

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	**RECOMMENDATION**	**DATE**	**REVIEWER**
Microbiology	Acceptable	5/1/09	Steven Donald
EES	Acceptable	9/2/10	M. Stock
Methods Validation	Not required		
Labeling	Acceptable	3/17/09	Beverly Weitzman
Bioequivalence	Acceptable	3/16/09	Farrar, Johnetta L
EA	Categorical exclusion	3/6/06	M. Farahani

Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. ____ Yes ___x_ No If no, explain reason(s) below: Minor amendment

The Chemistry Review for ANDA 78-208

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The application is approvable.

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)

Drug Substance:

Naphazoline Hydrochloride, USP manufactured by:
(b) (4)

Naphazoline Hydrochloride, USP is White to off-white crystalline powder. The pH is 5.0-6.6 and solution is clear and colorless. It is soluble in water.

DMF (b) (4) describes the synthesis of the drug substance Naphazoline Hydrochloride, USP. The DMF was reviewed by M. Farahani on February 4, 2008 and was found to be inadequate.

Pheniramine Maleate, USP manufactured by:
(b) (4)

Pheniramine Maleate, USP is a white fine crystalline powder. The melting point is 104°C-109°C.

DMF (b) (4) describes the synthesis of the drug substance Pheniramine Maleate, USP. The DMF was reviewed by M. Farahani on December 30, 2007 and was found to be inadequate.

Drug product: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%. Ophthalmic Solution temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair and dander.

Inactive ingredients in the formulation are: Hydroxypropyl methylcellulose, USP, Purified water, USP, Boric acid, NF, Sodium borate, NF, Sodium chloride, USP, Edetate disodium, USP, Benzalkonium chloride, USP (b) (4)

Following this page, 3 pages withheld in full (b)(4)

cc: ANDA 78- 208
ANDA DUP
Division File
Field Copy

Endorsements:

HFD-624/M.Farahani/9/20/10
HFD-627/J.Fan/9/20/10
HFD-617/T. Tran/9/20/10

V:\Chem I\Team 3\FIRMSAM\ Altaire \LTRS&REV\78208.R04.doc

TYPE OF LETTER: ANDA is approvable

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

/s/

MAHNAZ FARAHANI
09/21/2010

TRANG Q TRAN
09/21/2010

JAMES M FAN
09/21/2010

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	78-208
Drug Product Name	Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution/Drops
Strength(s)	Naphazoline HCl – 0.027% Pheniramine Maleate – 0.315%
Applicant Name	Altaire Pharmaceuticals, Inc.
Address	PO Box 849 311 West Lane Aquebogue, NY 11931
Applicant's Point of Contact	Mr. Martin Dalsing Phone: (970) 243 – 5490 Fax: (970) 243 – 5501 Email: marty@fdapproval.com
Contact's Telephone Number	631-722-5988
Contact's Fax Number	631-722-9683
Original Submission Date(s)	27 August 2007
Submission Date(s) of Amendment(s) Under Review	N/A
Reviewer	Johnetta L. Farrar, Ph.D.
OUTCOME DECISION	**INCOMPLETE**

1 EXECUTIVE SUMMARY

This application is for the **first generic** product of Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate, 0.315% Ophthalmic Solution/Drops. The firm, Altaire Pharmaceuticals, Inc., has requested a waiver of *in vivo* bioequivalence (BE) requirements based on Section 505 (j) of the Federal Food, Drug and Cosmetic Act for its test product, Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops. The reference-listed drug (RLD) drug product is Opcon-A® (Naphazoline HCl, 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb (NDA 20-065, Approval Date: 18 June 1994).

The current Division of Bioequivalence (DBE) recommendations for ophthalmic products (March 2008)[1] state that in order for an ophthalmic product to be considered for a waiver of *in vivo* BE study requirements under 21 CFR§ 320.22 (b) (1) the product should be qualitatively (Q1) and quantitatively (Q2) the same as the RLD product, including preservatives, buffers and thickening agents (exceptional excipients). In addition, the test product's physico-chemical properties (pH, specific gravity, osmolality, and viscosity) should be comparable with those of

[1] v:\firmsam (b) (4) Controls\070104.C.0107.mor.doc

the RLD. Pursuant to 21 CFR § 320.22 (b) (1), the criteria for waiver of evidence of *in vivo* bioavailability or bioequivalence are as follows:

"The drug product: (i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."

In case of any qualitative or quantitative differences in exceptional excipients, the Office of Generic Drugs (OGD) may accept for filling of an ANDA for an ophthalmic product under the 21 CFR § 314.94 (a) (9) (iv). However, the OGD may not approve such ANDA without a BE study (with a clinical endpoint) in order to demonstrate safety or efficacy.

The formulation of the test product is qualitatively but not quantitatively the same as the RLD product. There are differences in the (b) (4) between the two formulations.

Therefore, according to the current DBE policy[2], the firm's waiver request is denied at this time.

The DBE recommends the following options to the firm:

1) In order to gain approval for this ophthalmic product without a BE study, the firm should i) reformulate its test product to be Q1 and Q2 the same as the RLD product, and ii) submit comparative chemico-physical properties (e.g., specific gravity, pH, osmolality, and viscosity) for the newly formulated test product vs. RLD product.

2) If the firm decides not to reformulate the proposed test product, and selects to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), the firm is requested to conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. The firm may submit a protocol to the OGD for review prior to initiation of its study.

The application is **incomplete** with a deficiency.

[2] Division of Bioequivalence Review of ANDA # (b) (4) DFS Bioequivalence Review N (b) (4) N 000 28-Dec-2006.

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution
Reference Product	Opcon-A® (Naphazoline Hydrochloride 0.02675% % Pheniramine Maleate, 0.315% Ophthalmic Solution)
RLD Manufacturer	Bausch and Lomb
NDA No.	20-065
RLD Approval Date	18 June 1994
Indication[3]	Temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair, and dander.

3.2 PK/PD Information[3, 4]

Bioavailability	Naphazoline may be systemically absorbed from both the nasal mucosa and gastrointestinal tract after intranasal administration, resulting in systemic adverse effects, especially when excessive doses are used. After I.V. administration, serum concentrations of pheniramine between 231 and 894 ng/ml were reached.
Food Effect	Not applicable
Tmax	Naphazoline: N/A Following oral administration, peak serum concentrations between 173 and 274 ng/ml were reached after 1.0 to 2.5 hours.
Metabolism	Naphazoline: N/A Pheniramine has two major metabolites: N-desmethyl pheniramine and N-didesmethyl pheniramine.
Excretion	Naphazoline: N/A The amount of pheniramine excreted in the urine for up to 120 h varied between 5.7 and 11.6 mg and 10.2 and 13.2 mg after i.v. and oral administration respectively.
Half-life	Naphazoline: N/A The terminal half-life of pheniramine was estimated to range between 8 and 17 h (i.v.) and 16 and 19 h (oral).
Drug Specific Issues (if any)	None.

[3] FDA Drug Database. Labeling for Opcon-A. Last accessed: 25 November 2008. Drugdex® Drug Evaluations: Naphazoline. http://csi.micromedex.com/DKS/Data/DE/DE0566.HTM#03000000$$00$$; Last accessed: 19 November 2008.

[4] Witte, PU, et. al. "Pharmacokinetics of pheniramine (Avil) an metabolites in healthy subjects after oral and intravenous administration." International Journal of Clinical Pharmacology, Therapy and Toxicology Volume 1 (1985): 59-62.

3.3 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
Steady-state	No	--
In vitro dissolution	No	--
Waiver requests	Yes	1
BCS Waivers	No	--
Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	No	--

3.4 Formulation

Location in appendix	Section 4.1, Page 17
If a tablet, is the RLD scored?	N/A
If a tablet, is the test product biobatch scored	N/A
Is the formulation acceptable?	**FORMULATION INCOMPLETE**
If not acceptable, why?	The test and RLD formulations contain quantitative (Q2) differences.

3.5 Waiver Request(s)

Strengths for which waivers are requested	Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315%
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	**WAIVERS DENIED**
If not then why?	Pursuant to 21 CFR § 320.22 (b) (1), the Criteria for Waiver of evidence of *in vivo* bioavailability or bioequivalence is as follows: *"The drug product: (i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."* Since the test formulation contains differences (b) (4) (b) (4) as well as qualitative differences, the formulation is not considered quantitatively (Q2) the same as the RLD. The waiver, as requested, is denied.

3.6 Deficiency Comment

The test product and reference-listed drug (RLD) product formulations for Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops is qualitatively (Q1) but not quantitatively (Q2) the same.

3.7 Recommendations

1. The Division of Bioequivalence (DBE) does not agree that the information submitted by Altaire Pharmaceuticals, Inc. demonstrates that Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops met the requirements of Section 21 CFR § 320.22 (b) (1). The DBE recommends the waiver of bioequivalence testing be denied. Accordingly bioequivalence testing should be undertaken for the test product.

2. According to the current DBE policy, in order to gain approval for this ophthalmic product without a bioequivalence (BE) study, the firm should i) reformulate its test product to match qualitatively and quantitatively to the reference-listed drug (RLD) product, Opcon-A® (Naphazoline HCl, 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb, and ii) submit comparative chemico-physical properties (e.g., specific gravity, pH, osmolality, and viscosity) for the newly formulated test product vs. RLD product.

3. If the firm decides not to reformulate the proposed test product and selects to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), then the firm should conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products.

4. The application is incomplete.

The firm should be informed of the above deficiency comment and recommendations.

3.8 Comments for Other OGD Disciplines

Discipline	Comment
None	N/A

4 APPENDIX

4.1 Formulation Data (NOT FOR RELEASE UNDER FOIA)

Ingredient	Test Formulation	RLD Formulation[5]	Percentage Difference
(b) (4)	(b) (4)	(b) (4)	(b) (4)
Hydroxypropylmethylcellulose (b) (4) USP			
Boric Acid, NF			
Sodium Borate, NF			
Disodium Edetate, USP[7]			
Sodium Chloride, USP			
Naphazoline Hydrochloride, USP	0.02675%	0.02675%	--
Pheniramine Maleate, USP	0.315%	0.315%	--
Benzalkonium Chloride (b) (4) NF	0.01%[8]	0.01%	--

Is there an overage of the active pharmaceutical ingredient (API)?	No.
If the answer is yes, has the appropriate chemistry division been notified?	No.
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	No.
Comments on the drug product formulation:	Pursuant to 21 CFR § 320.22 (b) (1), the Criteria for Waiver of evidence of *in vivo* bioavailability or bioequivalence is as follows: *"The drug product:* *(i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."* Since the test formulation contains differences (b) (4), the formulation is not considered quantitatively (Q2) the same as the

[5] Formulation information obtained from the original Chemistry review of the NDA submission. Please see "RLD Formulation" in the Additional Attachments section of this review.
[6] Sodium Borate (b) (4)
[7] The RLD formulation contains "Edetate Disodium," whereas the test formulation contains "Disodium Edetate." Per the FDA Inactive Ingredient Guide, Edetate Disodium is the appropriate nomenclature.
(b) (4)

	RLD. The waiver, as requested, is denied.

Reviewer's Comments:

The differences in [redacted] between the test and RLD formulations are greater than [redacted] as shown above. [redacted]. Per the OGD Regulatory Support Staff (see Additional Attachments - Questions for ANDA 78-208 Formulation), the firm changed its formulation by excluding these pH adjusters. As a result, the application was acceptable for filing and is qualitatively (Q1) the same as the RLD. The current Division of Bioequivalence (DBE) recommendations for ophthalmic products (March 2008)[9] state that in order for an ophthalmic product to be considered for a waiver of *in vivo* BE study requirements under 21 CFR § 320.22 (b) (1) the product should be qualitatively (Q1) ***and*** quantitatively (Q2) the same as the RLD product, including preservatives, buffers and thickening agents (exceptional excipients). As a result, the waiver of bioequivalence testing is denied.

4.2 Detailed Regulatory History

According to the OGD Regulatory Support Staff, [redacted]

Also, per the OGD Regulatory Support Staff (see Additional Attachments - Questions for ANDA 78-208 Formulation), the test product [redacted]. As a result, the application was acceptable for filing and is qualitatively (Q1) the same as the RLD.

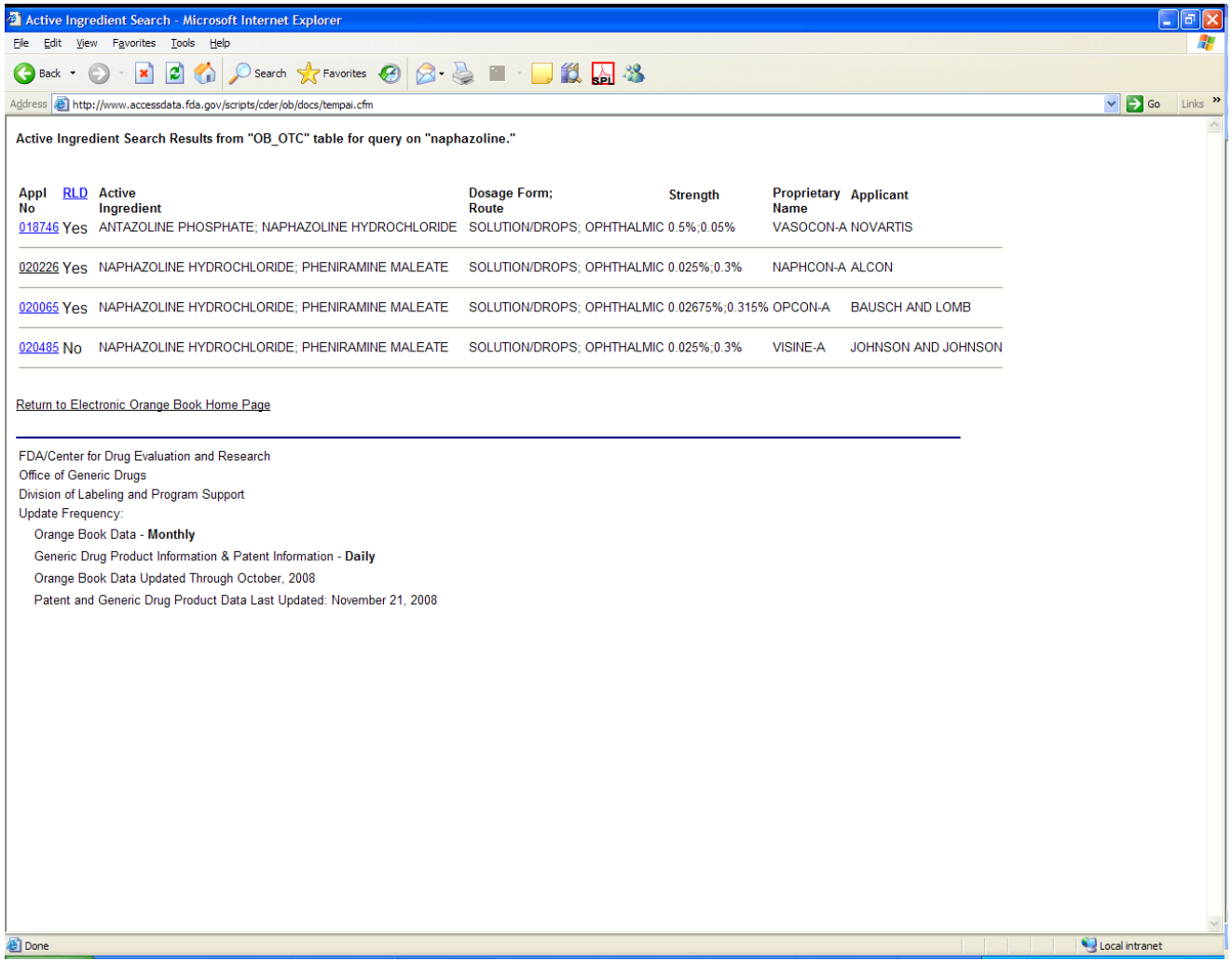
It should be noted that [redacted]. Per the OGD Regulatory Support Staff (see Additional Attachments - Questions for ANDA 78-208 Formulation), "the application was not accepted for filing until [redacted], as the inclusion was not an allowable change under 21 CFR § 314.94(a) (9) (iv), and a new exhibit batch was manufactured."

4.3 Consult Reviews

N/A

[9] v:\firmsam\[redacted]Controls\070104.C.0107.mor.doc
[10] DFS, Forms, ANDA Checklist Refuse to File CSO N 078208 N 000 AC 26-Jun-2006.
[11] DFS, Forms, ANDA Checklist General, CSO, N 078208 N 000 AC 27-Aug-2007.

4.4 Additional Attachments – Electronic Orange Book



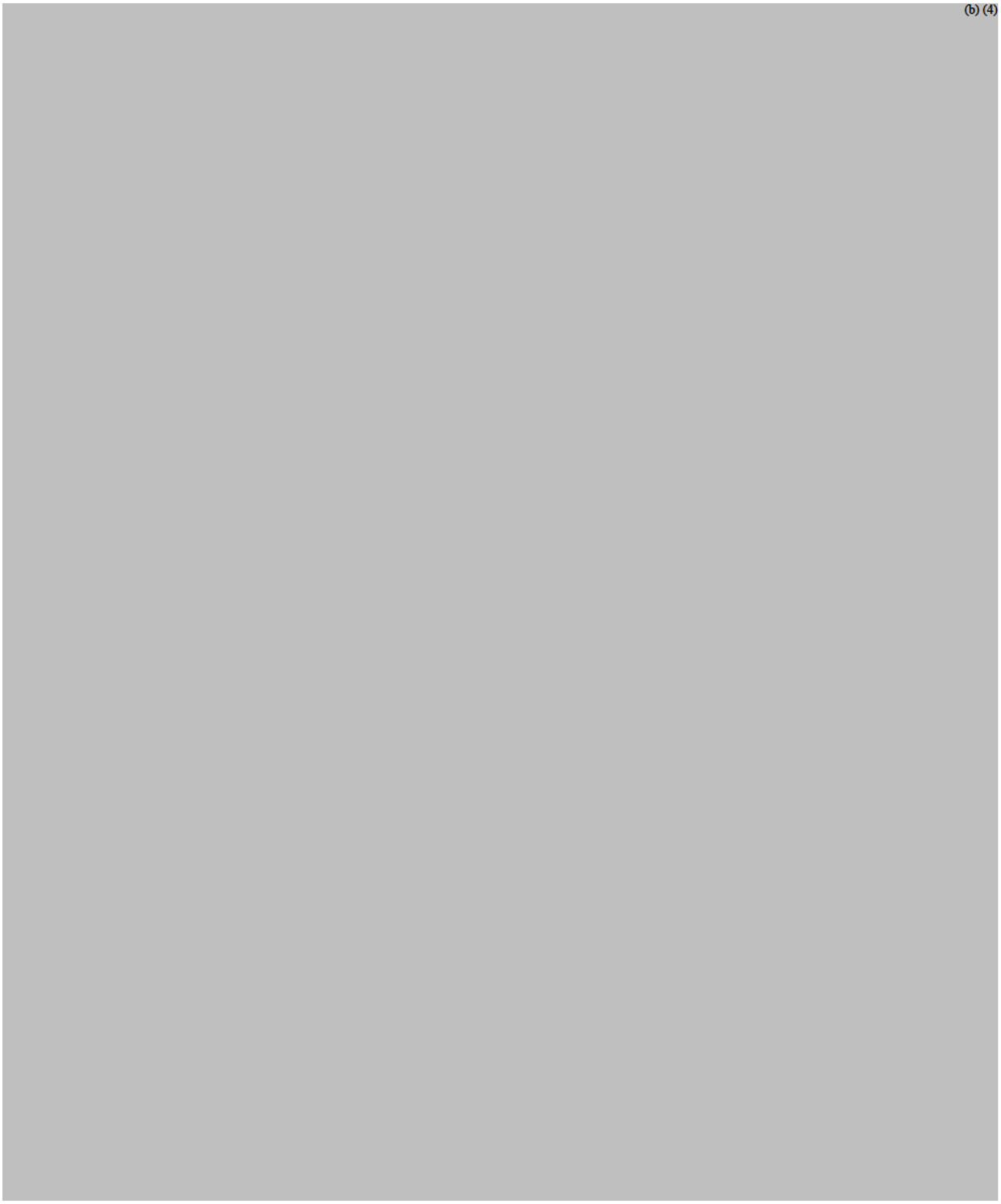
4.5 Additional Attachments –Formulation for NDA 20-065 Bausch and Lomb's Opcon-A

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 11:45 AM
To: Braddy, April; Farrar, Johnetta
Cc: Nguyen, Hoainhon T
Subject: FW: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

Attachments: Picture (Enhanced Metafile); Picture (Enhanced Metafile)

From: Rodriguez, Libaniel
Sent: Tuesday, December 02, 2008 11:33 AM
To: Nguyen, Hoainhon T; De, Swapan K
Subject: RE: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

(b) (4)



I hope this helps

Libaniel

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 10:28 AM
To: Rodriguez, Libaniel; De, Swapan K
Cc: Nguyen, Hoainhon T
Subject: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

Good morning,

We in the Division of Bioequivalence I, Office of Generic Drugs, are currently reviewing a First Generic version of Opcon-A (Naphazoline HCl, 0.027%, and Pheniramine Maleate, 0.315%, Drops (OTC). We would like to confirm the formulation of the innovator's product, for qualitative and quatitative comparison with the generic formulation. We have searched DFS and Enterprisesearch for the formulation information but could not locate any. The only source we found was COMIS database which is known to contain many errors.
We noticed your names in most recent chemistry reviews of the NDA and hope that you could assist us in obtaining the accurate and most updated formulation of Opcon-A, NDA 20065.

Thanks very much in advance for your help.

Hoainhon Nguyen Caramenico
Acting Deputy Director
Division of Bioequivalence I
Office of Generic Drugs
CDER/FDA
Telephone: 240-276-8804
Email: hoainhon.caramenico@fda.hhs.gov

4.6 Additional Attachments –Questions for ANDA 78-208 Formulation

From: Margand, Iain
Sent: Tuesday, December 02, 2008 1:49 PM
To: Nguyen, Hoainhon T; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta
Subject: RE: Questions for ANDA 78208 Formulation

Hi Hoainhon,

1. The first formulation on page 12 is the applicant final formulation and the second is a copy of the RLD package insert formulation.
2. The application was not accepted for filing until [redacted] (b) (4) as the inclusion was not an allowable change under 21 CFR 314.94(a)(9)(iv), and a new exhibit batch was manufactured. I took a look in the 3.1 jacket in which the applicant has stated [redacted] (b) (4) and committed to providing a new exhibit batch .
3. The COMIS formulation and the RLD package insert are the only two formulations used as references for the review of the application. I could not find a copy of the original RLD formulation in DFS.

Hope this helps.

Iain

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 12:50 PM
To: Margand, Iain; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta; Nguyen, Hoainhon T
Subject: RE: Questions for ANDA 78208 Formulation

Iain,
Thanks for your quick reply.

1. On page 12 of your checklist review (attached again for your reference), there are two formulations listed. Did you mean the TOP formulation was the TEST formulation (ANDA 78208)? The way the page was presented, it appeared that the TOP formulation belongs to Opcon A (as the name given right below the formulation table.). Please clarify/confirm whether the TOP formulation is the TEST or RLD (which I originally thought was the RLD formulation).

2. Please confirm that (b) (4) (b) (4) Our BE reviewer apparently looked at the original submission, and not any other amendments, and found the information on the (b) (4) (b) (4). This is where I got the information about (b) (4). However, I just now noticed that you have commented in your review that the (b) (4) in the amendment dated 5/6/2007.

3. Besides the COMIS and the RLD labeling information, were there other sources of information you relied on for your information of the RLD product formulation? We have just recently obtained the original RLD formulation submitted in 1990 from the NDA chemist and just want to make sure that there has been no change in the RLD formulation since then.

Thanks very much,
Hoai
<< File: 78208 ANDA Checklist and Opcon A Formulation.pdf >>

From: Margand, Iain
Sent: Tuesday, December 02, 2008 12:30 PM
To: Nguyen, Hoainhon T; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta
Subject: RE: Questions for ANDA 78208 Formulation

Hello Hoainhon,

Can you tell me what formulation you are referring to in your e-mail (b) (4) (b) (4)? The two RLD formulations listed on the checklist are from COMIS and the RLD package insert, neither list (b) (4) as part of the formulation. The third formulation is the applicants'. The application was accepted prior to the change in policy that an ophthalmic must be Q1/Q2 to the RLD.

Iain

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 12:10 PM
To: Margand, Iain; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta; Nguyen, Hoainhon T
Subject: Questions for ANDA 78208 Formulation

Iain and Martin,
I have noticed that your ANDA Checklist review dated October 26, 2007 for the

above ANDA (RLD is Opcon A Ophthamic Drops, NDA 20065) included a formulation of the RLD product. (Thanks for pointing out in the review that the COMIS formulation information is INCORRECT!) This formulation in your checklist review is different from the original formulation of Opcon A submitted in 1995 for approval. It appears that Bausch and Lomb has changed its formulation over the years. Could you please let us know where ***the source*** of your RLD formulation information (including ***the date***, if possible)? Based on this "newer" RLD formulation, it appears that the test and RLD products are Q1 and Q2 match (b) (4) (b) (4) Did you file this ANDA because of 21 CFR 314.94 (9)(iv) even though we currently do not approve ophthalmic drug products that are not Q1 and Q2 match, unless there is a BE study with clinical endpoints? Thanks very much in advance for your clarification.
Hoai

<< File: 78208 ANDA Checklist and Opcon A Formulation.pdf >>

BIOEQUIVALENCE DEFICIENCIES

ANDA:	78-208
APPLICANT:	Altaire Pharmaceuticals, Inc.
DRUG PRODUCT:	Naphazoline HCl & Pheniramine Maleate (0.027% & 0.315%) Ophthalmic Solution/Drops

The Division of Bioequivalence (DBE) has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiency has been identified:

Your requested waiver of in vivo bioequivalence (BE) study requirements for your test product, Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops does not meet the requirements set forth in Section 21 CFR § 320.22 (b) (1). Your test product formulation is qualitatively (Q1) but not quantitatively (Q2) the same as the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb. Therefore, the waiver request is denied.

The DBE currently recommends the following options:

a. In order to obtain a waiver of in vivo bioequivalence testing for your test product under 21 CFR § 320.22(b) (1):

   i) Please reformulate your test product to match qualitatively and quantitatively to the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution);

   ii) In addition, please submit comparative chemico-physical data, which should include but not be limited to pH, specific gravity, osmolality and viscosity, for the newly reformulated test product versus RLD product.

b. Alternatively, if you decide not to reformulate the current test formulation and to have the current test formulation be considered under 21 CFR § 314.94 (a) (9) (iv), please conduct a bioequivalence study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. You may

submit a protocol to the Office of Generic Drugs prior to initiation of your study, for review and comments.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

4.7 Outcome Page

ANDA: 78-208

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
6899	8/27/2007	Other	Waiver Ophthalmic Solution	1	1
				Bean Total:	1

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

/s/

Johnetta Farrar
12/4/2008 09:47:34 AM
BIOPHARMACEUTICS

April Braddy
12/10/2008 07:28:23 AM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
12/11/2008 11:42:02 AM
BIOPHARMACEUTICS
For Dale P. Conner, Pharm. D., Director, Division of Bioequivalence I

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	78-208
Drug Product Name	Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution/Drops
Strength(s)	Naphazoline HCl – 0.027% Pheniramine Maleate – 0.315%
Applicant Name	Altaire Pharmaceuticals, Inc.
Address	PO Box 849 311 West Lane Aquebogue, NY 11931
Applicant's Point of Contact	Mr. Martin Dalsing Phone: (970) 243 – 5490 Fax: (970) 243 – 5501 Email: marty@fdapproval.com
Contact's Telephone Number	631-722-5988
Contact's Fax Number	631-722-9683
Original Submission Date(s)	27 August 2007
Submission Date(s) of Amendment(s) Under Review	02 February 2009 03 February 2009[1]
Reviewer	Johnetta L. Farrar, Ph.D.
OUTCOME DECISION	**INCOMPLETE**

1 EXECUTIVE SUMMARY

This is a review of an amendment to a waiver request.

This application is for the **first generic** product of Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate, 0.315% Ophthalmic Solution/Drops. In the *previous* (original) submission (27 August 2007)[2], the firm, Altaire Pharmaceuticals, Inc., requested a waiver of *in vivo* bioequivalence (BE) requirements based on Section 505 (j) of the Federal Food, Drug and Cosmetic Act for its test product, Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops. The reference-listed drug (RLD) drug product is Opcon-A® (Naphazoline HCl, 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb (NDA 20-065, Approval Date: 18 June 1994).

[1] Per COMIS (an internal database, last accessed 11 February 2009), the firm has submitted a response to the cited bioequivalence deficiencies (letter date: 02 February 2009). In a separate submission, the firm has also submitted a cover letter to accompany the aforementioned response to cited deficiencies (letter date: 03 February 2009).

[2] DFS: Review: Bioequivalence Review; Biopharmaceutics; N 078208 N 000 AC 27-Aug-2007.

However, the waiver request was denied at that time due to the fact that the formulation of the firm's test product was not qualitatively (Q1) or quantitatively (Q2) the same as the RLD product. There was a difference of (b) (4) in the concentrations of (b) (4) between the test and RLD formulations.

Based on the current DBE recommendations for ophthalmic products, the firm was provided with the following options:

Option # 1

In order to gain approval for this ophthalmic product without a BE study by obtaining a waiver of in vivo bioequivalence testing for its testing product under 21 CFR§ 320.22 (b) (1), the firm should i) reformulate its test product to be Q1 and Q2 the same as the RLD product, and ii) submit comparative chemico-physical properties (e.g., specific gravity, pH, osmolality, and viscosity) for the newly formulated test product vs. RLD product.

Option # 2

If the firm decided not to reformulate the proposed test product, and selected to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), the firm was requested to conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. The firm was advised they could submit a protocol to the OGD for review prior to initiation of its study.

The firm chose option # 1. However, the firm's **reformulated** test product is Q1 but not Q2 the same as the RLD product. There is a difference of (b) (4) in the (b) (4) between the two formulations.

Therefore, the DBE recommends the following options to the firm:

1) In order to gain approval for this ophthalmic product without a BE study, the firm should i) reformulate (b) (4) in its test product to be Q1 and Q2 the same as the RLD product, and ii) submit comparative chemico-physical properties (e.g., specific gravity, pH, osmolality, and viscosity) for the newly formulated test product vs. RLD product. The firm may submit its reformulated composition for review prior to conducting testing for determination of chemico-physical properties of the reformulated product.

2) If the firm decides not to reformulate the proposed test product, and selects to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), the firm is requested to conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. The firm may submit a protocol to the OGD for review prior to initiation of its study.

The application is **incomplete** with a deficiency.

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution
Reference Product	Opcon-A® (Naphazoline Hydrochloride 0.02675% % Pheniramine Maleate, 0.315% Ophthalmic Solution)
RLD Manufacturer	Bausch and Lomb
NDA No.	20-065
RLD Approval Date	18 June 1994
Indication[3]	Temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair, and dander.

3.2 PK/PD Information[3, 4]

Bioavailability	Naphazoline may be systemically absorbed from both the nasal mucosa and gastrointestinal tract after intranasal administration, resulting in systemic adverse effects, especially when excessive doses are used. After I.V. administration, serum concentrations of pheniramine between 231 and 894 ng/ml were reached.
Food Effect	Not applicable
Tmax	Naphazoline: N/A Following oral administration, peak serum concentrations between 173 and 274 ng/ml were reached after 1.0 to 2.5 hours.
Metabolism	Naphazoline: N/A Pheniramine has two major metabolites: N-desmethyl pheniramine and N-didesmethyl pheniramine.
Excretion	Naphazoline: N/A The amount of pheniramine excreted in the urine for up to 120 h varied between 5.7 and 11.6 mg and 10.2 and 13.2 mg after i.v. and oral administration respectively.
Half-life	Naphazoline: N/A The terminal half-life of pheniramine was estimated to range between 8 and 17 h (i.v.) and 16 and 19 h (oral).
Drug Specific Issues (if any)	None.

[3] FDA Drug Database. Labeling for Opcon-A. Last accessed: 25 November 2008. Drugdex® Drug Evaluations: Naphazoline. http://csi micromedex.com/DKS/Data/DE/DE0566.HTM#03000000$$00$$; Last accessed: 19 November 2008.

[4] Witte, PU, et. al. "Pharmacokinetics of pheniramine (Avil) an metabolites in healthy subjects after oral and intravenous administration." International Journal of Clinical Pharmacology, Therapy and Toxicology Volume 1 (1985): 59-62.

3.3 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
Steady-state	No	--
In vitro dissolution	No	--
Waiver requests	No	--
BCS Waivers	No	--
Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	Yes	1

3.4 Formulation

Location in appendix	Section 4.1, Page 17
If a tablet, is the RLD scored?	N/A
If a tablet, is the test product biobatch scored	N/A
Is the formulation acceptable?	**FORMULATION IS INCOMPLETE**
If not acceptable, why?	The test and RLD formulations contain quantitative (Q2) differences.

3.5 Waiver Request(s)

Strengths for which waivers are requested	Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315%
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	**WAIVERS DENIED**
If not then why?	Pursuant to 21 CFR § 320.22 (b) (1), the Criteria for Waiver of evidence of *in vivo* bioavailability or bioequivalence is as follows: *"The drug product: (i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."* Since the test formulation contains differences (b) (4) (b) (4), the formulation is not considered quantitatively (Q2) the same as the RLD. The waiver, as requested, is denied.

3.6 Firm's Current Responses to DBE Deficiencies

DBE's Previous Deficiency Comment No. 1 (See the review of the submission dated 27 August 2007)**:**

The DBE currently recommends the following options:

> *a. In order to obtain a waiver of in vivo bioequivalence testing for your test product under 21 CFR § 320.22(b) (1):*
>
> *i) Please reformulate your test product to match qualitatively and quantitatively to the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution);*
>
> *ii) In addition, please submit comparative chemico-physical data, which should include but not be limited to pH, specific gravity, osmolality and viscosity, for the newly reformulated test product versus RLD product.*
>
> *b. Alternatively, if you decide not to reformulate the current test formulation and to have the current test formulation be considered under 21 CFR § 314.94 (a) (9) (iv), please conduct a bioequivalence study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. You may submit a protocol to the Office of Generic Drugs prior to initiation of your study, for review and comments.*

Firm's Current Response No. 1:

> *"Altaire has reformulated the Proposed Drug Product "Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution" to qualitatively and quantitatively match the Reference Drug Product Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution). Attached hereto at "Appendix A" is a copy of the proposed reformulation, and what follows is a review of the reformulation process and results."*
>
> The firm has also submitted "*a comparison of the chemico-physical properties of the formulation of the Reference Drug Product and the reformulation of the Proposed Drug Product."*

Reviewer's Comment (NOT FOR RELEASE UNDER FOIA):

The difference (b) (4) between the test and RLD formulations is (b) (4). The current Division of Bioequivalence (DBE) recommendations for ophthalmic products (March 2008)[5] state that in order for an ophthalmic product to be considered for a waiver of *in vivo* BE study

[5] v:\firmsam(b) (4)Controls\070104.C.0107.mor.doc

requirements under 21 CFR § 320.22 (b) (1) the product should be qualitatively (Q1) ***and*** quantitatively (Q2) the same as the RLD product, including preservatives, buffers and thickening agents (exceptional excipients). The firm did submit comparative chemico-physical data. However, the data were not reviewed since the formulation of the test product is not Q2 the same as the RLD product. As a result, the waiver of bioequivalence testing is denied.

3.7 Deficiency Comment

The **reformulated** test product and reference-listed drug (RLD) product formulations for Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops is qualitatively (Q1) but not quantitatively (Q2) the same.

Therefore, the following options will be provided to the firm:

1. In order to gain approval for this ophthalmic product without a BE study, the firm should i) reformulate (b) (4) in its test product to be quantitatively the same as the concentration in the RLD product and ii) submit comparative (newly formulated test product vs. RLD product) matching data on specific gravity, pH, osmolality, and viscosity. The comparative data on specific gravity, pH, osmolality, tonicity and viscosity for the test and RLD products should be provided using the Exhibit test lot, and two (2) other production lots, if available, of the test product, and 3 commercial lots of the RLD product. The measurement should be done in triplicate for each lot tested. However, the firm is advised to submit the reformulated composition for review prior to conducting testing for characterizing the chemico-physical properties of the reformulation product in comparison with the RLD product.

2. If the firm decides not to accept the above stated recommendation and selects to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), the firm is requested to conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. The firm may submit a protocol to the OGD for review prior to initiation of their study.

3.8 Recommendations

1. The Division of Bioequivalence (DBE) does not agree that the information submitted by Altaire Pharmaceuticals, Inc. demonstrates that it's Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops met the requirements of Section 21 CFR § 320.22 (b) (1). The DBE recommends the waiver of bioequivalence testing be denied. Accordingly, *in vivo* bioequivalence testing may be undertaken for the test product.

2. According to the current DBE policy, in order to gain approval for this ophthalmic product without a bioequivalence (BE) study, the firm should i) reformulate [redacted] (b) (4) in its test product to be quantitatively the same as the concentration in the reference-listed drug (RLD) product, Opcon-A® (Naphazoline HCl, 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb, and ii) submit comparative chemico-physical properties (e.g., specific gravity, pH, osmolality, and viscosity) for the newly formulated test product vs. RLD product.

3. If the firm decides not to reformulate the proposed test product and selects to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), then the firm should conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products.

4. The application is incomplete.

The firm should be informed of the above deficiency comment and recommendations.

3.9 Comments for Other OGD Disciplines

Discipline	Comment
None	N/A

4 APPENDIX

4.1 Formulation Data (NOT FOR RELEASE UNDER FOIA)

Ingredient	Test Formulation	RLD Formulation[6]	Percentage Difference
(b) (4)	(b) (4)	(b) (4)	(b) (4)
Hydroxypropylmethylcellulose (b) (4) USP			
Boric Acid, NF			
Sodium Borate, NF			
Disodium Edetate, USP[8]			
Sodium Chloride, USP			
Naphazoline Hydrochloride, USP	0.02675%	0.02675%	--
Pheniramine Maleate, USP	0.315%	0.315%	--
Benzalkonium Chloride (b) (4) NF	0.01%[9]	0.01%	--

Is there an overage of the active pharmaceutical ingredient (API)?	No.
If the answer is yes, has the appropriate chemistry division been notified?	No.
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	No.
Comments on the drug product formulation:	Pursuant to 21 CFR § 320.22 (b) (1), the criteria for waiver of evidence of *in vivo* bioavailability or bioequivalence is as follows: *"The drug product:* *(i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."* Since the test formulation contains

[6] Formulation information obtained from the original Chemistry review of the NDA submission. Please see "RLD Formulation" in the Additional Attachments section of this review.

[7] Sodium Borate (b) (4)

[8] The RLD formulation contains "Edetate Disodium," whereas the test formulation contains "Disodium Edetate." Per the FDA Inactive Ingredient Guide, Edetate Disodium is the appropriate nomenclature.

(b) (4)

	differences in (b) (4) the formulation is not considered quantitatively (Q2) the same as the RLD. The waiver, as requested, is denied.

Reviewer's Comments:

Please see the Reviewer's Comments noted in Section 3.6.

4.2 Detailed Regulatory History

According to the OGD Regulatory Support Staff, (b) (4)

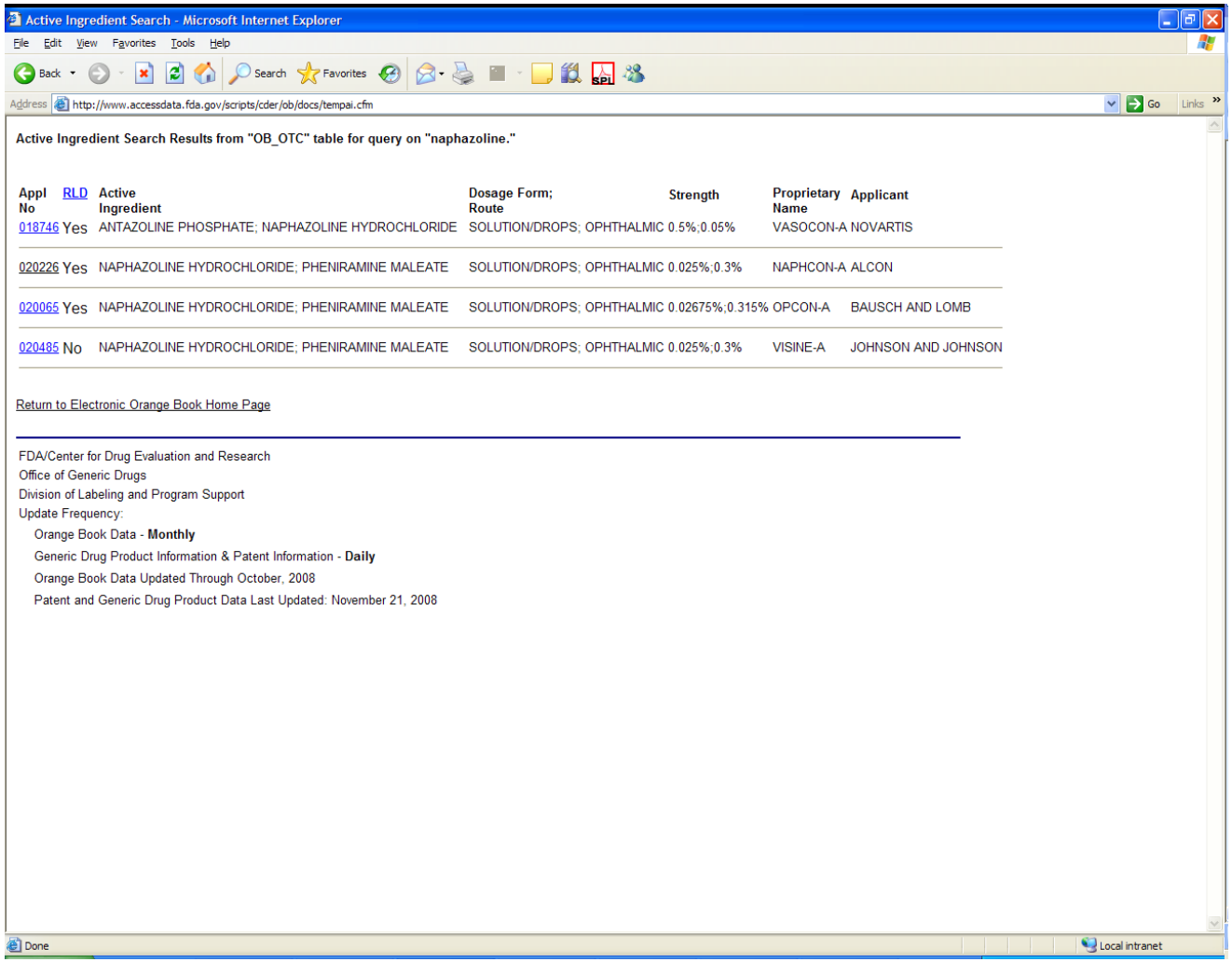
Initially, the firm's test formulation (b) (4) Per the OGD Regulatory Support Staff (see Additional Attachments - Questions for ANDA 78-208 Formulation) [12], the firm changed its formulation (b) (4). As a result, the application was acceptable for filing [314.94 (a) (9) (iv)] and is qualitatively (Q1) the same as the RLD.

4.3 Consult Reviews

N/A

[10] DFS, Forms, ANDA Checklist Refuse to File CSO N 078208 N 000 AC 26-Jun-2006.
[11] DFS: Review; MIC AP Line unknown Alta; Microbiologist; N 078208 N 000 15-Mar-2006.
[12] DFS, Forms, ANDA Checklist General, CSO, N 078208 N 000 AC 27-Aug-2007.

4.4 Additional Attachments – Electronic Orange Book



Active Ingredient Search - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites

Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/tempai.cfm Go Links

Active Ingredient Search Results from "OB_OTC" table for query on "naphazoline."

Appl No	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
018746	Yes	ANTAZOLINE PHOSPHATE; NAPHAZOLINE HYDROCHLORIDE	SOLUTION/DROPS; OPHTHALMIC	0.5%;0.05%	VASOCON-A	NOVARTIS
020226	Yes	NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE	SOLUTION/DROPS; OPHTHALMIC	0.025%;0.3%	NAPHCON-A	ALCON
020065	Yes	NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE	SOLUTION/DROPS; OPHTHALMIC	0.02675%;0.315%	OPCON-A	BAUSCH AND LOMB
020485	No	NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE	SOLUTION/DROPS; OPHTHALMIC	0.025%;0.3%	VISINE-A	JOHNSON AND JOHNSON

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through October, 2008
Patent and Generic Drug Product Data Last Updated: November 21, 2008

Done Local intranet

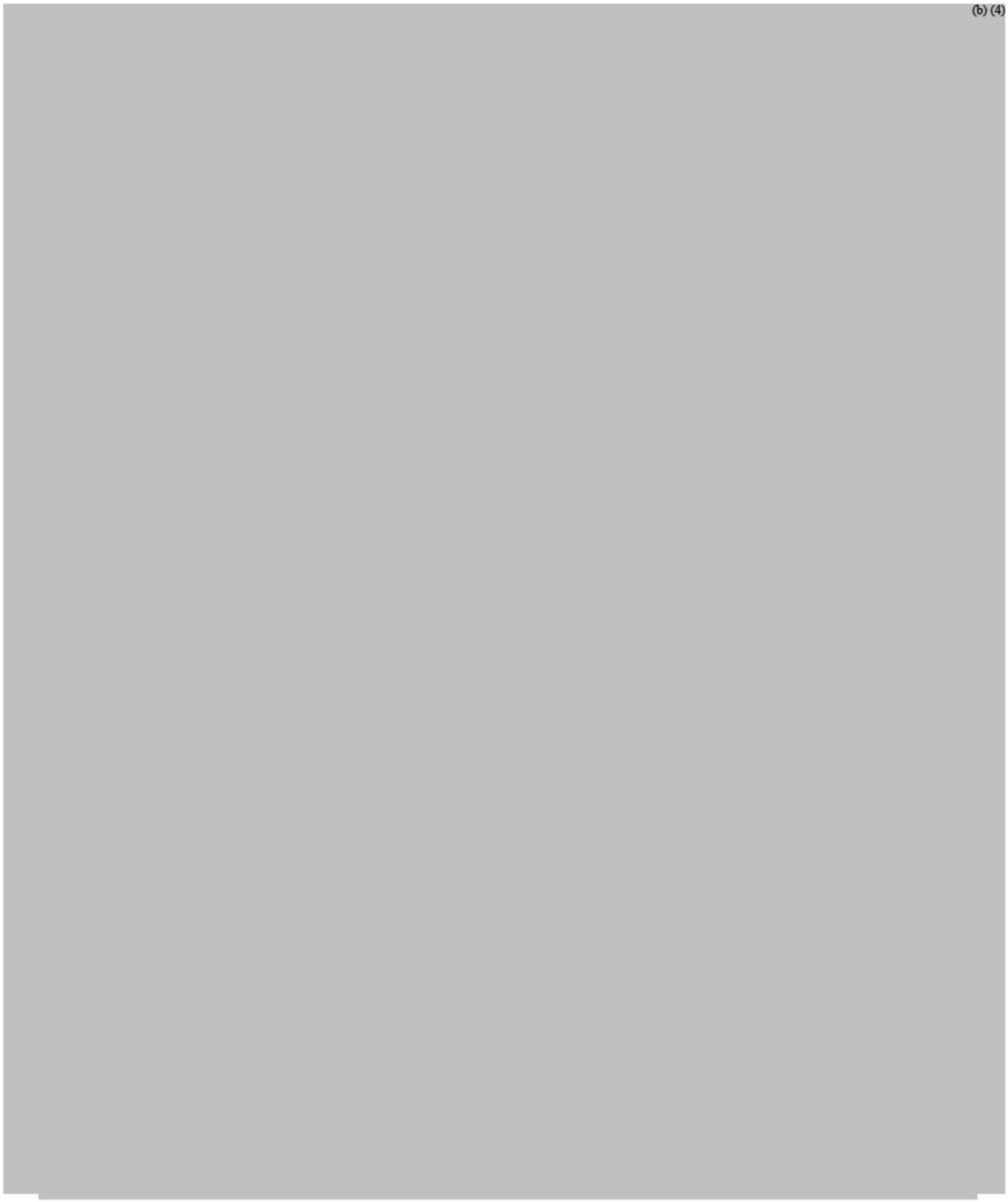
4.5 Additional Attachments –Formulation for NDA 20-065 Bausch and Lomb's Opcon-A

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 11:45 AM
To: Braddy, April; Farrar, Johnetta
Cc: Nguyen, Hoainhon T
Subject: FW: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

Attachments: Picture (Enhanced Metafile); Picture (Enhanced Metafile)

From: Rodriguez, Libaniel
Sent: Tuesday, December 02, 2008 11:33 AM
To: Nguyen, Hoainhon T; De, Swapan K
Subject: RE: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

(b) (4)



I hope this helps

Libaniel

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 10:28 AM
To: Rodriguez, Libaniel; De, Swapan K
Cc: Nguyen, Hoainhon T
Subject: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

Good morning,

We in the Division of Bioequivalence I, Office of Generic Drugs, are currently reviewing a First Generic version of Opcon-A (Naphazoline HCl, 0.027%, and Pheniramine Maleate, 0.315%, Drops (OTC). We would like to confirm the formulation of the innovator's product, for qualitative and quantitative comparison with the generic formulation. We have searched DFS and Enterprisesearch for the formulation information but could not locate any. The only source we found was COMIS database which is known to contain many errors.
We noticed your names in most recent chemistry reviews of the NDA and hope that you could assist us in obtaining the accurate and most updated formulation of Opcon-A, NDA 20065.

Thanks very much in advance for your help.

Hoainhon Nguyen Caramenico
Acting Deputy Director
Division of Bioequivalence I
Office of Generic Drugs
CDER/FDA
Telephone: 240-276-8804
Email: hoainhon.caramenico@fda.hhs.gov

4.6 Additional Attachments –Questions for ANDA 78-208 Formulation

From: Margand, Iain
Sent: Tuesday, December 02, 2008 1:49 PM
To: Nguyen, Hoainhon T; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta
Subject: RE: Questions for ANDA 78208 Formulation

Hi Hoainhon,

1. The first formulation on page 12 is the applicant final formulation and the second is a copy of the RLD package insert formulation.
2. The application was not accepted for filing until (b) (4) as the inclusion was not an allowable change under 21 CFR 314.94(a)(9)(iv), and a new exhibit batch was manufactured. I took a look in the 3.1 jacket in which the applicant has stated (b) (4) and committed to providing a new exhibit batch .
3. The COMIS formulation and the RLD package insert are the only two formulations used as references for the review of the application. I could not find a copy of the original RLD formulation in DFS.

Hope this helps.

Iain

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 12:50 PM
To: Margand, Iain; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta; Nguyen, Hoainhon T

Subject: RE: Questions for ANDA 78208 Formulation

Iain,
Thanks for your quick reply.

1. On page 12 of your checklist review (attached again for your reference), there are two formulations listed. Did you mean the TOP formulation was the TEST formulation (ANDA 78208)? The way the page was presented, it appeared that the TOP formulation belongs to Opcon A (as the name given right below the formulation table.). Please clarify/confirm whether the TOP formulation is the TEST or RLD (which I originally thought was the RLD formulation).

2. Please confirm that (b) (4) (b) (4) Our BE reviewer apparently looked at the original submission, and not any other amendments, and found the information on the (b) (4) (b) (4). This is where I got the information about (b) (4) However, I just now noticed that you have commented in your review that the (b) (4) in the amendment dated 5/6/2007.

3. Besides the COMIS and the RLD labeling information, were there other sources of information you relied on for your information of the RLD product formulation? We have just recently obtained the original RLD formulation submitted in 1990 from the NDA chemist and just want to make sure that there has been no change in the RLD formulation since then.

Thanks very much,
Hoai
<< File: 78208 ANDA Checklist and Opcon A Formulation.pdf >>

From: Margand, Iain
Sent: Tuesday, December 02, 2008 12:30 PM
To: Nguyen, Hoainhon T; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta
Subject: RE: Questions for ANDA 78208 Formulation

Hello Hoainhon,

Can you tell me what formulation you are referring to in your e-mail (b) (4) (b) (4)? The two RLD formulations listed on the checklist are from COMIS and the RLD package insert, neither list (b) (4) as part of the formulation. The third formulation is the applicants'. The application was accepted prior to the change in policy that an ophthalmic must be Q1/Q2 to the RLD.

Iain

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 12:10 PM
To: Margand, Iain; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta; Nguyen, Hoainhon T
Subject: Questions for ANDA 78208 Formulation

Iain and Martin,
I have noticed that your ANDA Checklist review dated October 26, 2007 for the above ANDA (RLD is Opcon A Ophthamic Drops, NDA 20065) included a formulation of the RLD product. (Thanks for pointing out in the review that the COMIS

formulation information is INCORRECT!) This formulation in your checklist review is different from the original formulation of Opcon A submitted in 1995 for approval. It appears that Bausch and Lomb has changed its formulation over the years. Could you please let us know where ***the source*** of your RLD formulation information (including ***the date***, if possible)? Based on this "newer" RLD formulation, it appears that the test and RLD products are Q1 and Q2 match (b) (4) (b) (4) Did you file this ANDA because of 21 CFR 314.94 (9)(iv) even though we currently do not approve ophthalmic drug products that are not Q1 and Q2 match, unless there is a BE study with clinical endpoints?
Thanks very much in advance for your clarification.
Hoai

<< File: 78208 ANDA Checklist and Opcon A Formulation.pdf >>

BIOEQUIVALENCE DEFICIENCY

ANDA:	78-208
APPLICANT:	Altaire Pharmaceuticals, Inc.
DRUG PRODUCT:	Naphazoline HCl & Pheniramine Maleate (0.027% & 0.315%) Ophthalmic Solution/Drops

The Division of Bioequivalence (DBE) has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiency has been identified:

Your **reformulated** Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops is now qualitatively (Q1) but not quantitatively (Q2) the same as the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb. The amount of (b) (4) in your reformulated product is not the same as that in the RLD product. Therefore, the waiver request is still denied at this time.

As stated in our previous deficiency letter to you, the DBE currently recommends the following options:

1. In order to obtain a waiver of in vivo bioequivalence testing for your test product under 21 CFR § 320.22(b)(1):

    a) Please reformulate (b) (4) in your test product to be quantitatively the same as in the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), and, in addition

    b) Please submit comparative chemico-physical data, which should include but not be limited to pH, specific gravity, osmolality and viscosity, for the newly reformulated test product versus RLD product. The comparative data on specific gravity, pH, osmolality, tonicity and viscosity for the test and RLD products should be provided using the Exhibit (reformulated) test lot, and two (2) other production lots, if available, of the test product, and 3 commercial lots of the

RLD product. The measurement should be done in triplicate for each lot tested. It is advisable that you submit the reformulated composition for review prior to conducting additional testing to characterize the chemico-physical properties of the reformulated product in comparison with the RLD product.

2. Alternatively, if you decide not to reformulate the current test formulation and to have the current test formulation be considered under 21 CFR § 314.94 (a) (9) (iv), please conduct a bioequivalence study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. You may submit a protocol to the Office of Generic Drugs prior to initiation of your study, for review and comments.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

4.7 Outcome Page

ANDA: 78-208

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
7507	2/2/2009	Other	Waiver Ophthalmic Solution	1	1
				Bean Total:	1

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

/s/

Johnetta Farrar
2/13/2009 02:54:43 PM
BIOPHARMACEUTICS

Hongling Zhang
2/13/2009 02:59:00 PM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
2/13/2009 05:02:38 PM
BIOPHARMACEUTICS
For Dale P. Conner, Pharm. D., Director, Division of Bioequivalence I

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	78-208
Drug Product Name	Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution/Drops
Strength(s)	Naphazoline HCl – 0.027% Pheniramine Maleate – 0.315%
Applicant Name	Altaire Pharmaceuticals, Inc.
Address	PO Box 849 311 West Lane Aquebogue, NY 11931
Applicant's Point of Contact	Mr. Martin Dalsing Phone: (970) 243 – 5490 Fax: (970) 243 – 5501 Email: marty@fdapproval.com
Contact's Telephone Number	631-722-5988
Contact's Fax Number	631-722-9683
Original Submission Date(s)	27 August 2007
Submission Date(s) of Amendment(s) Under Review	02 February 2009 03 February 2009[1] **Current: 03 March 2009**
Reviewer	Johnetta L. Farrar, Ph.D.
OUTCOME DECISION	**ACCEPTABLE**

1 EXECUTIVE SUMMARY

This is a review of the ***second*** amendment to a waiver request.

This application is for the **first generic** product of Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate, 0.315% Ophthalmic Solution/Drops. In the original submission (27 August 2007)[2], the firm, Altaire Pharmaceuticals, Inc., requested a waiver of *in vivo* bioequivalence (BE) requirements based on Section 505 (j) of the Federal Food, Drug and Cosmetic Act for its test product, Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops. The reference-listed drug (RLD) drug product is Opcon-A® (Naphazoline HCl, 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb (NDA 20-065, Approval Date: 18 June 1994, over-the-counter product).

[1] Per COMIS (an internal database, last accessed 11 February 2009), the firm has submitted a response to the cited bioequivalence deficiencies (letter date: 02 February 2009). In a separate submission, the firm has also submitted a cover letter to accompany the aforementioned response to cited deficiencies (letter date: 03 February 2009).

[2] DFS: Review: Bioequivalence Review; Biopharmaceutics; N 078208 N 000 AC 27-Aug-2007.

However, the waiver request was denied at that time due to the fact that the formulation of the firm's test product was qualitatively (Q1) but not quantitatively (Q2) the same as the RLD product. There was a difference of (b) (4) in the concentrations (b) (4) between the test and RLD formulations.

Based on the current DBE recommendations for ophthalmic products, the firm was provided with the following options:

Option # 1

In order to gain approval for this ophthalmic product without a BE study by obtaining a waiver of in vivo bioequivalence testing for its testing product under 21 CFR§ 320.22 (b) (1), the firm should i) reformulate its test product to be Q1 and Q2 the same as the RLD product, and ii) submit comparative chemico-physical properties (e.g., specific gravity, pH, osmolality, and viscosity) for the newly formulated test product vs. RLD product.

Option # 2

If the firm decided not to reformulate the proposed test product, and selected to have the test product be considered under 21 CFR § 314.94 (a) (9) (iv), the firm was requested to conduct a BE study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. The firm was advised they could submit a protocol to the OGD for review prior to initiation of its study.

In the *first* amendment submission dated 02 February 2009[3], the firm, Altaire Pharmaceuticals, Inc., chose option # 1 and **reformulated** its test product. However, it was still was denied at that time due to the fact that the formulation of the firm's test product was still not quantitatively (Q2) the same as the RLD product. There was a difference of (b) (4) in the concentration of (b) (4) between the reformulated test and RLD formulations. Therefore, the firm was once again provided with the above two options.

In the *current* amendment, the firm again chose option # 1. The firm's **reformulated** test product is both Q1 and Q2 the same as the RLD product. There are no differences (b) (4) in the quantity of any active or inactive ingredient between the two formulations. In addition, the test product's physico-chemical properties (pH, specific gravity, osmolality, and viscosity) are comparable with those of the RLD.

Based on the above information, the waiver request is granted under 21 CFR§ 320.22 (b) (1). As a result the Division of DBE (DBE) deems the test product, Naphazoline Hydrochloride (HCl), 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops to be bioequivalent to the RLD drug product, Opcon-A® (Naphazoline HCl, 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb.

Therefore, the application is **acceptable** with no deficiencies.

[3] DFS: Review: Bioequivalence Review; Biopharmaceutics; N 078208 N 000 AC 27-Aug-2007.

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution
Reference Product	Opcon-A® (Naphazoline Hydrochloride 0.02675% % Pheniramine Maleate, 0.315% Ophthalmic Solution)
RLD Manufacturer	Bausch and Lomb
NDA No.	20-065
RLD Approval Date	18 June 1994
Indication[4]	Temporarily relieves itching and redness caused by pollen, ragweed, grass, animal hair, and dander.

3.2 PK/PD Information[4, 5]

Bioavailability	Naphazoline may be systemically absorbed from both the nasal mucosa and gastrointestinal tract after intranasal administration, resulting in systemic adverse effects, especially when excessive doses are used. After I.V. administration, serum concentrations of pheniramine between 231 and 894 ng/ml were reached.
Food Effect	Not applicable
Tmax	Naphazoline: N/A Following oral administration, peak serum concentrations between 173 and 274 ng/ml were reached after 1.0 to 2.5 hours.
Metabolism	Naphazoline: N/A Pheniramine has two major metabolites: N-desmethyl pheniramine and N-didesmethyl pheniramine.
Excretion	Naphazoline: N/A The amount of pheniramine excreted in the urine for up to 120 h varied between 5.7 and 11.6 mg and 10.2 and 13.2 mg after i.v. and oral administration respectively.
Half-life	Naphazoline: N/A The terminal half-life of pheniramine was estimated to range between 8 and 17 h (i.v.) and 16 and 19 h (oral).
Drug Specific Issues (if any)	None.

[4] FDA Drug Database. Labeling for Opcon-A. Last accessed: 25 November 2008. Drugdex® Drug Evaluations: Naphazoline. http://csi micromedex.com/DKS/Data/DE/DE0566.HTM#03000000$$00$$; Last accessed: 19 November 2008.

[5] Witte, PU, et. al. "Pharmacokinetics of pheniramine (Avil) an metabolites in healthy subjects after oral and intravenous administration." International Journal of Clinical Pharmacology, Therapy and Toxicology Volume 1 (1985): 59-62.

3.3 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	No	--
Single-dose fed	No	--
Steady-state	No	--
In vitro dissolution	No	--
Waiver requests	No	--
BCS Waivers	No	--
Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	Yes	1

3.4 Formulation

Location in appendix	Section 4.1, Page 17
If a tablet, is the RLD scored?	N/A
If a tablet, is the test product biobatch scored	N/A
Is the formulation acceptable?	**FORMULATION IS ACCEPTABLE**
If not acceptable, why?	The test and RLD formulations contain no qualitative (Q1) or quantitative (Q2) differences.

3.5 Waiver Request(s)

Strengths for which waivers are requested	Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315%
Proportional to strength tested in vivo?	N/A
Is dissolution acceptable?	N/A
Waivers granted?	**WAIVER GRANTED**
If not then why?	Pursuant to 21 CFR § 320.22 (b) (1), the Criteria for Waiver of evidence of *in vivo* bioavailability or bioequivalence is as follows: *"The drug product: (i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."* Since the test formulation contains no differences in (b) (4) the formulation is considered qualitatively (Q1) and quantitatively (Q2) the same as the RLD. The waiver, as requested, is granted.

3.6 Firm's Current Responses to DBE Deficiencies

DBE's Previous Deficiency Comment No. 1 (See the review of the submission dated 02 February 2009)**:**

The DBE currently recommends the following options:

a. In order to obtain a waiver of in vivo bioequivalence testing for your test product under 21 CFR § 320.22(b) (1):

i) Please reformulate your test product to match qualitatively and quantitatively to the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution);

ii) In addition, please submit comparative chemico-physical data, which should include but not be limited to pH, specific gravity, osmolality and viscosity, for the newly reformulated test product versus RLD product.

b. Alternatively, if you decide not to reformulate the current test formulation and to have the current test formulation be considered under 21 CFR § 314.94 (a) (9) (iv), please conduct a bioequivalence study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. You may submit a protocol to the Office of Generic Drugs prior to initiation of your study, for review and comments.

Firm's Current Response No. 1:

"Altaire has further reformulated the Proposed Drug Product "Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution" to qualitatively and quantitatively match the Reference Drug Product Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), in accordance with the deficiency indicated in the February 17, 2009 deficiency letter. Attached hereto at "Appendix A" is a copy of the proposed r-reformulation, and what follows is a review of the reformulation process and results."

The firm has also submitted "*a comparison of the chemico-physical properties of the formulation of the Reference Drug Product and the reformulation of the Proposed Drug Product."*

Reviewer's Comment (NOT FOR RELEASE UNDER FOIA):

(b) (4)

The current Division of Bioequivalence (DBE) recommendations for ophthalmic products (March

2008)[6] state that in order for an ophthalmic product to be considered for a waiver of *in vivo* BE study requirements under 21 CFR § 320.22 (b) (1) the product should be qualitatively (Q1) ***and*** quantitatively (Q2) the same as the RLD product, including preservatives, buffers and thickening agents (exceptional excipients). The firm also submitted comparative chemico-physical data. This submitted data is acceptable. As a result, the waiver of bioequivalence testing is granted.

3.7 Deficiency Comment

None.

3.8 Recommendations

1. The Division of Bioequivalence (DBE) finds that the formulation of the Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops is acceptable under the Section 21 CFR § 320.22 (b) (1) and the waiver request of *in vivo* bioequivalence requirements is granted under the same regulation provision.

2. The DBE deems the test product Naphazoline HCl, 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops manufactured by Alcon Altaire Pharmaceuticals, Inc., to be bioequivalent to the reference product, Opcon-A® (naphazoline HCl, 0.02675% & pheniramine maleate 0.315%) Sterile Ophthalmic Solution manufactured by Bausch and Lomb.

The firm should be informed of the above recommendations.

3.9 Comments for Other OGD Disciplines

Discipline	Comment
None	N/A

[6] v:\firmsam (b) (4) Controls\070104.C.0107.mor.doc

4 APPENDIX

4.1 Formulation Data (NOT FOR RELEASE UNDER FOIA)

Ingredient	Test Formulation	RLD Formulation[7]	Percentage Difference
(b) (4)	(b) (4)	(b) (4)	(b) (4)
Hydroxypropylmethylcellulose (b) (4) USP			
Boric Acid, NF			
Sodium Borate, NF			
Disodium Edetate, USP[9]			
Sodium Chloride, USP			
Naphazoline Hydrochloride, USP	0.02675%	0.02675%	--
Pheniramine Maleate, USP	0.315%	0.315%	--
Benzalkonium Chloride (b) (4) NF	0.01%[10]	0.01%	--

Is there an overage of the active pharmaceutical ingredient (API)?	No.
If the answer is yes, has the appropriate chemistry division been notified?	No.
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	No.
Comments on the drug product formulation:	Pursuant to 21 CFR § 320.22 (b) (1), the criteria for waiver of evidence of *in vivo* bioavailability or bioequivalence is as follows: *"The drug product:* *(i) Is a parental solution intended solely for administration by injection, or an ophthalmic or otic solution; and (ii) Contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application or abbreviated new drug application."* Since the test formulation contains no

[7] Formulation information obtained from the original Chemistry review of the NDA submission. Please see "RLD Formulation" in the Additional Attachments section of this review.
[8] Sodium Borate (b) (4)
[9] The RLD formulation contains "Edetate Disodium," whereas the test formulation contains "Disodium Edetate." Per the FDA Inactive Ingredient Guide, Edetate Disodium is the appropriate nomenclature (b) (4)

	differences in (b) (4) the formulation is considered qualitatively (Q1) and quantitatively (Q2) the same as the RLD. The waiver, as requested, is granted.

Reviewer's Comments:

Please see the Reviewer's Comments noted in Section 3.6.

4.2 Comparative Physico-Chemical Data[11]

(b) (4)

[redacted]

Reviewer's Comments: The firm has shown the comparable physicochemical properties in pH, osmolality, viscosity and specific gravity for three lots of the reference product

[11] Provided by the firm in the current submission.

and two lots of the test product. The firm submitted the data in triplicate for each lot. The data, as shown above, is similar and comparable. Although the firm only provided the results for two lots of its test product, the data is acceptable.

Based on the above data, the firm's comparable physicochemical data is **acceptable**.

4.3 Detailed Regulatory History[3]

According to the OGD Regulatory Support Staff, (b) (4)

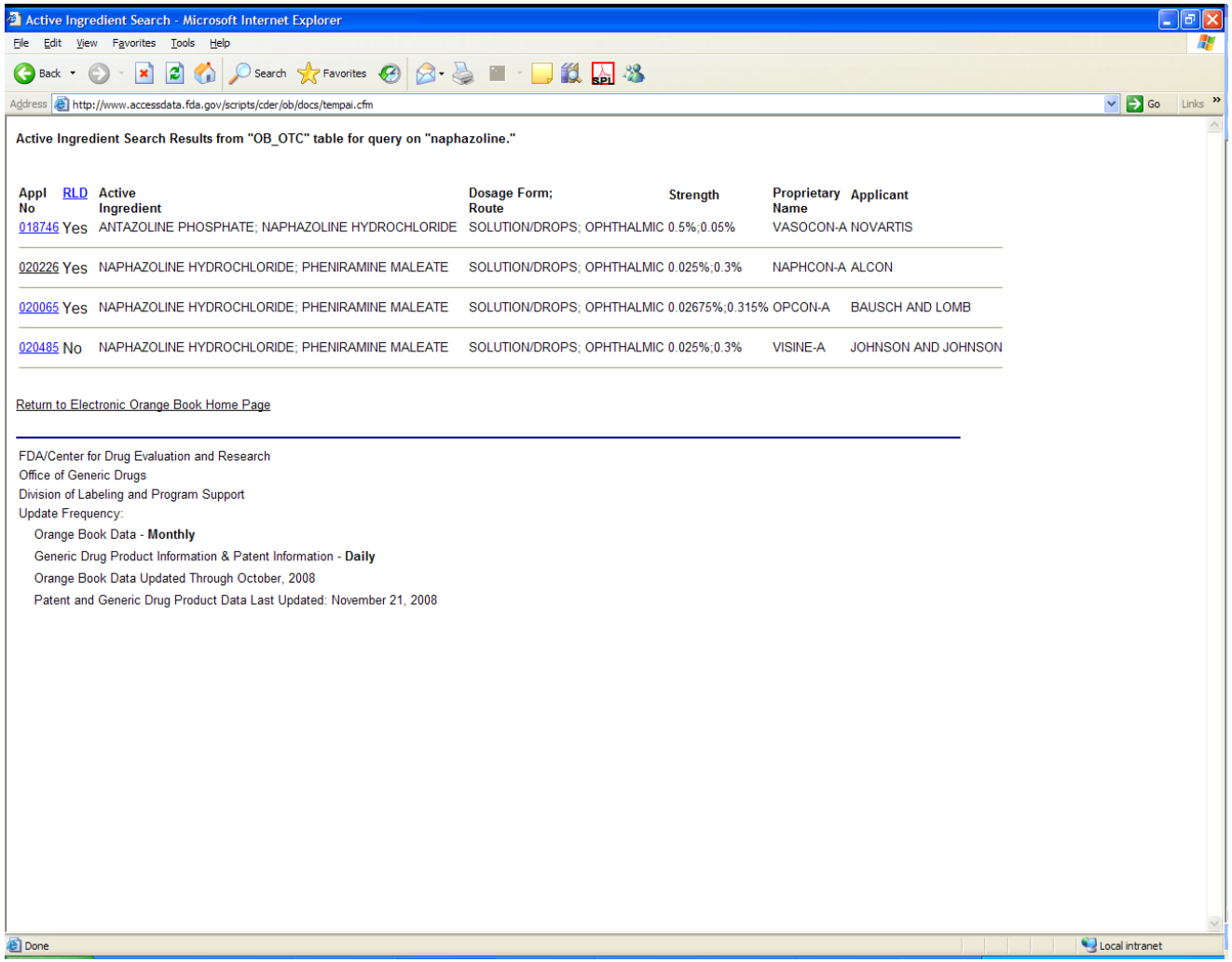
Initially, the firm's test formulation contained (b) (4) (b) (4) Per the OGD Regulatory Support Staff (see Additional Attachments - Questions for ANDA 78-208 Formulation) [14], the firm changed its formulation (b) (4) As a result, the application was acceptable for filing [314.94 (a) (9) (iv)] and is qualitatively (Q1) the same as the RLD.

4.4 Consult Reviews

N/A

[12] DFS, Forms, ANDA Checklist Refuse to File CSO N 078208 N 000 AC 26-Jun-2006.
[13] DFS: Review; (b) (4); Microbiologist; N 078208 N 000 15-Mar-2006.
[14] DFS, Forms, ANDA Checklist General, CSO, N 078208 N 000 AC 27-Aug-2007.

4.5 Additional Attachments – Electronic Orange Book



Active Ingredient Search - Microsoft Internet Explorer

File Edit View Favorites Tools Help

Back Search Favorites

Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/tempai.cfm

Go Links

Active Ingredient Search Results from "OB_OTC" table for query on "naphazoline."

Appl No	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
018746	Yes	ANTAZOLINE PHOSPHATE; NAPHAZOLINE HYDROCHLORIDE	SOLUTION/DROPS; OPHTHALMIC	0.5%;0.05%	VASOCON-A	NOVARTIS
020226	Yes	NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE	SOLUTION/DROPS; OPHTHALMIC	0.025%;0.3%	NAPHCON-A	ALCON
020065	Yes	NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE	SOLUTION/DROPS; OPHTHALMIC	0.02675%;0.315%	OPCON-A	BAUSCH AND LOMB
020485	No	NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE	SOLUTION/DROPS; OPHTHALMIC	0.025%;0.3%	VISINE-A	JOHNSON AND JOHNSON

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through October, 2008
Patent and Generic Drug Product Data Last Updated: November 21, 2008

Done Local intranet

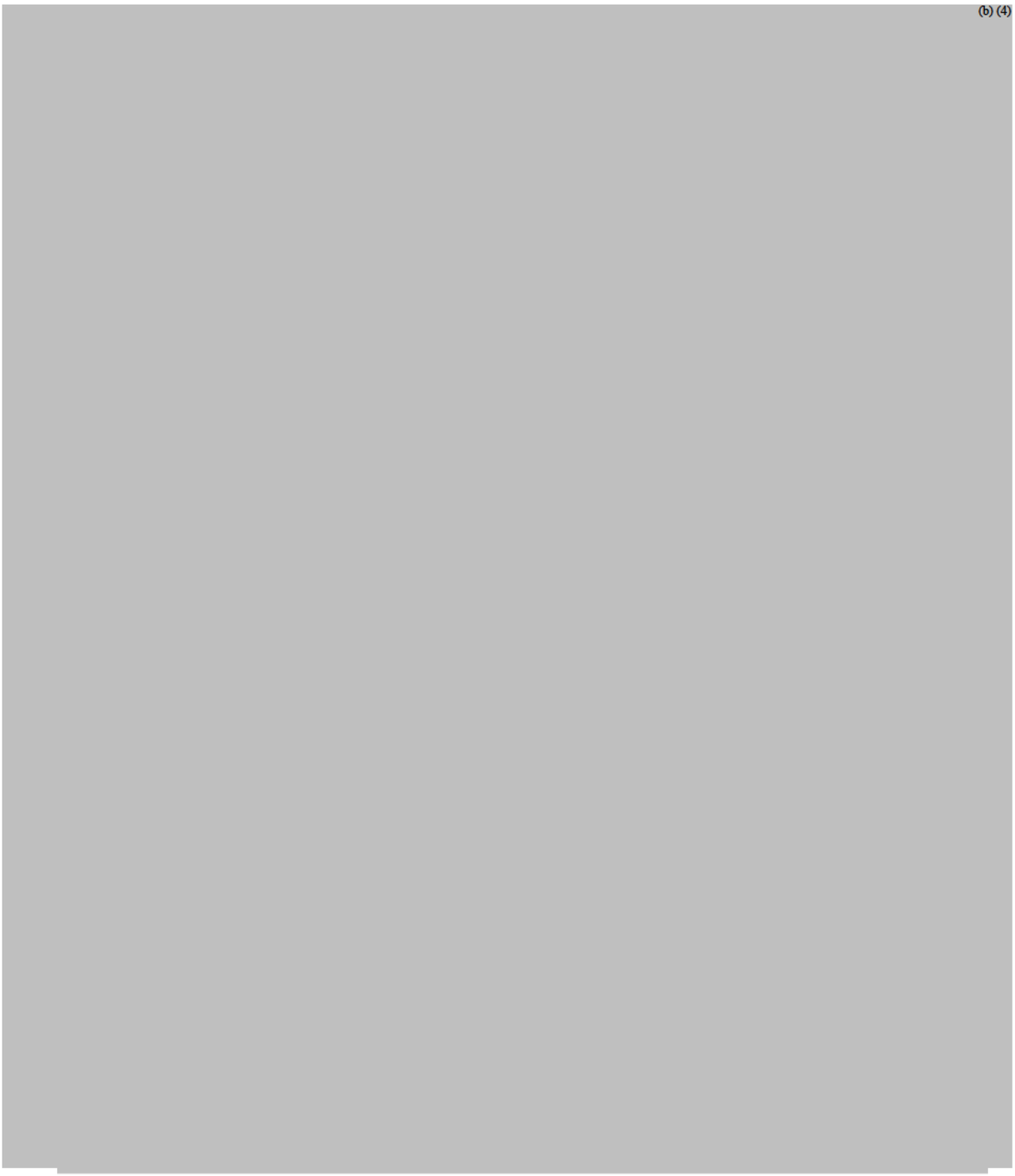
4.6 Additional Attachments –Formulation for NDA 20-065 Bausch and Lomb's Opcon-A

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 11:45 AM
To: Braddy, April; Farrar, Johnetta
Cc: Nguyen, Hoainhon T
Subject: FW: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

Attachments: Picture (Enhanced Metafile); Picture (Enhanced Metafile)

From: Rodriguez, Libaniel
Sent: Tuesday, December 02, 2008 11:33 AM
To: Nguyen, Hoainhon T; De, Swapan K
Subject: RE: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

(b) (4)



I hope this helps

Libaniel

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 10:28 AM
To: Rodriguez, Libaniel; De, Swapan K
Cc: Nguyen, Hoainhon T
Subject: Formulation for NDA 20065 Bausch and Lomb's Opcon-A

Good morning,

We in the Division of Bioequivalence I, Office of Generic Drugs, are currently reviewing a First Generic version of Opcon-A (Naphazoline HCl, 0.027%, and Pheniramine Maleate, 0.315%, Drops (OTC). We would like to confirm the formulation of the innovator's product, for qualitative and quantitative comparison with the generic formulation. We have searched DFS and Enterprisesearch for the formulation information but could not locate any. The only source we found was COMIS database which is known to contain many errors.
We noticed your names in most recent chemistry reviews of the NDA and hope that you could assist us in obtaining the accurate and most updated formulation of Opcon-A, NDA 20065.

Thanks very much in advance for your help.

Hoainhon Nguyen Caramenico
Acting Deputy Director
Division of Bioequivalence I
Office of Generic Drugs
CDER/FDA
Telephone: 240-276-8804
Email: hoainhon.caramenico@fda.hhs.gov

4.7 Additional Attachments –Questions for ANDA 78-208 Formulation

From: Margand, Iain
Sent: Tuesday, December 02, 2008 1:49 PM
To: Nguyen, Hoainhon T; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta
Subject: RE: Questions for ANDA 78208 Formulation

Hi Hoainhon,

1. The first formulation on page 12 is the applicant final formulation and the second is a copy of the RLD package insert formulation.
2. The application was not accepted for filing until (b) (4) as the inclusion was not an allowable change under 21 CFR 314.94(a)(9)(iv), and a new exhibit batch was manufactured. I took a look in the 3.1 jacket in which the applicant has stated (b) (4) and committed to providing a new exhibit batch.
3. The COMIS formulation and the RLD package insert are the only two formulations used as references for the review of the application. I could not find a copy of the original RLD formulation in DFS.

Hope this helps.

Iain

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 12:50 PM
To: Margand, Iain; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta; Nguyen, Hoainhon T

Subject: RE: Questions for ANDA 78208 Formulation

Iain,
Thanks for your quick reply.

1. On page 12 of your checklist review (attached again for your reference), there are two formulations listed. Did you mean the TOP formulation was the TEST formulation (ANDA 78208)? The way the page was presented, it appeared that the TOP formulation belongs to Opcon A (as the name given right below the formulation table.). Please clarify/confirm whether the TOP formulation is the TEST or RLD (which I originally thought was the RLD formulation).

2. Please confirm that (b) (4) (b) (4) Our BE reviewer apparently looked at the original submission, and not any other amendments, and found the information on the (b) (4) (b) (4). This is where I got the information about (b) (4). However, I just now noticed that you have commented in your review that the (b) (4) in the amendment dated 5/6/2007.

3. Besides the COMIS and the RLD labeling information, were there other sources of information you relied on for your information of the RLD product formulation? We have just recently obtained the original RLD formulation submitted in 1990 from the NDA chemist and just want to make sure that there has been no change in the RLD formulation since then.

Thanks very much,
Hoai
<< File: 78208 ANDA Checklist and Opcon A Formulation.pdf >>

From: Margand, Iain
Sent: Tuesday, December 02, 2008 12:30 PM
To: Nguyen, Hoainhon T; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta
Subject: RE: Questions for ANDA 78208 Formulation

Hello Hoainhon,

Can you tell me what formulation you are referring to in your e-mail (b) (4) (b) (4) The two RLD formulations listed on the checklist are from COMIS and the RLD package insert, neither list (b) (4) as part of the formulation. The third formulation is the applicants'. The application was accepted prior to the change in policy that an ophthalmic must be Q1/Q2 to the RLD.

Iain

From: Nguyen, Hoainhon T
Sent: Tuesday, December 02, 2008 12:10 PM
To: Margand, Iain; Shimer, Martin
Cc: Braddy, April; Farrar, Johnetta; Nguyen, Hoainhon T
Subject: Questions for ANDA 78208 Formulation

Iain and Martin,
I have noticed that your ANDA Checklist review dated October 26, 2007 for the above ANDA (RLD is Opcon A Ophthalmic Drops, NDA 20065) included a formulation of the RLD product. (Thanks for pointing out in the review that the

COMIS formulation information is INCORRECT!) This formulation in your checklist review is different from the original formulation of Opcon A submitted in 1995 for approval. It appears that Bausch and Lomb has changed its formulation over the years. Could you please let us know where ***the source*** of your RLD formulation information (including ***the date***, if possible)? Based on this "newer" RLD formulation, it appears that the test and RLD products are Q1 and Q2 match (b) (4) (b) (4) Did you file this ANDA because of 21 CFR 314.94 (9) (iv) even though we currently do not approve ophthalmic drug products that are not Q1 and Q2 match, unless there is a BE study with clinical endpoints?
Thanks very much in advance for your clarification.
Hoai

<< File: 78208 ANDA Checklist and Opcon A Formulation.pdf >>

BIOEQUIVALENCE COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:	78-208
APPLICANT:	Altaire Pharmaceuticals, Inc.
DRUG PRODUCT:	Naphazoline HCl & Pheniramine Maleate (0.027% & 0.315%) Ophthalmic Solution/Drops

The Division of Bioequivalence has completed its review and has no further questions at this time.

Please note that the bioequivalence comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

4.8 Outcome Page

ANDA: 78-208

Productivity:

ID	***Letter Date***	***Productivity Category***	***Sub Category***	***Productivity***	***Subtotal***
7722	3/3/2009	Other	Waiver Ophthalmic Solution	1	1
				Bean Total:	1

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

/s/

Johnetta Farrar
3/16/2009 01:10:44 PM
BIOPHARMACEUTICS

April Braddy
3/16/2009 01:15:03 PM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
3/16/2009 11:49:15 PM
BIOPHARMACEUTICS
For Dale P. Conner, Pharm. D., Director, Division of Bioequivalence I

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

MICROBIOLOGY REVIEWS

Product Quality Microbiology Review

08/15/2008

ANDA: 78-208

Drug Product Name

Proprietary:

Non-proprietary: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

Drug Product Priority Classification:

Review Number: 1

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
03/15/06*	03/16/2006	N/A	08/15/2008
06/26/06*	06/29/06	N/A	08/15/2008
08/27/07	08/28/08	N/A	08/15/2008

*Refused to File

Submission History (for amendments only)

Applicant/Sponsor

Name: Altaire Pharmaceuticals, Inc.

Address: P. O. Box 849
311 West Lane
Aquebogue, NY 11931

U.S. Agent:

Name: Medvice Consulting, Inc.

Address: 2214 Sanford Dr., Suite B7
Grand Junction, CO 81505

Representative: Mr. Martin Dalsing,

Telephone: 970 243 5490, Fax: 970 243 5501

Name of Reviewer: Steven P. Donald

Conclusion: The submission **is not recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original ANDA

2. SUBMISSION PROVIDES FOR: Initial marketing of a sterile drug product

3. MANUFACTURING SITE: Altaire Pharmaceuticals, Inc.
311 West Lane, PO BOX 849 Aquebogue, NY 11931

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Sterile solution, topical, ophthalmic, Pheniramine malate 0.315%, Naphazoline HCl 0.027%, multi-dose, packaged as 0.5 oz. fill in a 15 cc bottle and a 1.0 oz. fill in a 30 cc bottle

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: N/A

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: None

filename: 78-208.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –Drug product is (b) (4) (b) (4) into sterile 15 and 30 ml bottles.

B. Brief Description of Microbiology Deficiencies - (b) (4)

C. Assessment of Risk Due to Microbiology Deficiencies - The safety risk associated with the microbiology deficiencies is considered high.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Microbiologist / Steven P. Donald, M.S.
Microbiology Team Leader/Lynne Ensor, Ph.D.

C. CC Block
cc: Field Copy

Following this page, 11 pages withheld in full (b)(4)

H. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 78-208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

A. Microbiology Deficiencies:

1. Regarding Composition of the Drug Product:
   a. Please identify (b) (4)

2. (b) (4)

3.

4.

Following this page, 1 page withheld in full (b)(4)

(b) (4)

8.

9.

10.

11.

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. For future submissions and ease of review, please consult the Agency's 1994 "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products".

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Steven P Donald
9/19/2008 11:51:40 AM
MICROBIOLOGIST

Bonnie McNeal
9/19/2008 12:18:30 PM
MICROBIOLOGIST
Checked for correct file and submission links only. All ok.

Lynne Ensor
9/19/2008 01:16:40 PM
MICROBIOLOGIST

Product Quality Microbiology Review

08/15/2008

ANDA: 78-208

Drug Product Name

Proprietary:

Non-proprietary: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

Drug Product Priority Classification:

Review Number: 2

Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
10/16/08	10/21/2008	N/A	10/30/2008

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
03/15/06*		
06/26/06*		
08/27/07	1	08/15/2008

*Refused to File

Applicant/Sponsor

Name: Altaire Pharmaceuticals, Inc.

Address: P. O. Box 849
311 West Lane
Aquebogue, NY 11931

U.S. Agent:

Name: Medvice Consulting, Inc.

Address: 2214 Sanford Dr., Suite B7
Grand Junction, CO 81505

Representative: Mr. Martin Dalsing,
Telephone: 970 243 5490, Fax: 970 243 5501

Name of Reviewer: Steven P. Donald

Conclusion: The submission **is not recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. **1.** **TYPE OF SUBMISSION:** ANDA Amendment,

2. **SUBMISSION PROVIDES FOR:** Response to microbiology deficiency letter.

3. **MANUFACTURING SITE:** Altaire Pharmaceuticals, Inc.
311 West Lane, PO BOX 849 Aquebogue, NY 11931

4. **DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:** Sterile solution, topical, ophthalmic, Pheniramine malate 0.315%, Naphazoline HCl 0.027%, multi-dose, packaged as 0.5 oz. fill in a 15 cc bottle and a 1.0 oz. fill in a 30 cc bottle

5. **METHOD(S) OF STERILIZATION:** (b) (4)

6. **PHARMACOLOGICAL CATEGORY:** N/A

B. **SUPPORTING/RELATED DOCUMENTS:** None

C. **REMARKS:** None

filename: 78-208a1.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –Drug product is (b) (4) (b) (4) filled into sterile 15 and 30 ml bottles.

B. Brief Description of Microbiology Deficiencies - (b) (4)

C. Assessment of Risk Due to Microbiology Deficiencies -
The safety risk associated with the microbiology deficiencies is considered high.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Microbiologist / Steven P. Donald, M.S.
Microbiology Team Leader/Lynne Ensor, Ph.D.

C. CC Block
cc: Field Copy

Following this page, 23 pages withheld in full (b)(4)

H. LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 78-208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

Microbiology Deficiencies:

1. (b) (4)

2.

3.

Following this page, 1 page withheld in full (b)(4)

6. (b) (4)

7.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Steven P Donald
11/21/2008 05:09:19 PM
MICROBIOLOGIST

Bonnie McNeal
11/21/2008 06:26:33 PM
MICROBIOLOGIST
Checked for correct file and submission link. Both ok.

Lynne Ensor
11/24/2008 07:01:27 AM
MICROBIOLOGIST

Product Quality Microbiology Review

01/28/2009

ANDA: 78-208

Drug Product Name
Proprietary: N/A
Non-proprietary: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%
Drug Product Priority Classification: N/A

Review Number: 3
Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
01/13/2009	01/15/2009	N/A	01/22/09

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
08/27/07	1	08/15/08
10/16/2008	2	08/15/2008

Applicant/Sponsor
Name: Altaire Pharmaceuticals, Inc.
Address: P. O. Box 849
311 West Lane
Aquebogue, NY 11931
U.S. Agent:
Name: Medvice Consulting, Inc.
Address: 2214 Sanford Dr., Suite B7
Grand Junction, CO 81505
Representative: Mr. Martin Dalsing,
Telephone: 970 243 5490, Fax: 970 243 5501

Name of Reviewer: Steven P. Donald

Conclusion: The submission is **not recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original Amendment

2. SUBMISSION PROVIDES FOR: Information in response to deficiency letter, dated November 24, 2008, addressing microbiological issues in review #2.

3. MANUFACTURING SITE: Altaire Pharmaceuticals, Inc.
311 West Lane, PO BOX 849 Aquebogue, NY 11931

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Sterile solution, topical, ophthalmic, Pheniramine malate 0.315%, Naphazoline HCl 0.027%, multi-dose, packaged as 0.5 oz. fill in a 15 cc bottle and a 1.0 oz. fill in a 30 cc bottle

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: N/A

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: On 02/06/09 I spoke with Michael Sawaya of Altaire Pharmaceuticals, Inc., in a telephone conversation regarding (b) (4) He is providing new (b) (4) information for the next amendment.

filename: 78-208a2.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability – The submission is **not recommended** for approval on the basis of sterility assurance. Specific comments and deficiencies are provided in the "Product Quality Microbiology Assessment" and "List of Microbiology Deficiencies and Comments" sections.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –Drug solution is (b) (4) (b) (4) filled into sterile 15 and 30 ml bottles.

B. Brief Description of Microbiology Deficiencies- (b) (4)

C. Assessment of Risk Due to Microbiology Deficiencies -
The safety risk associated with the microbiology deficiencies is considered low.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Microbiologist / Steven P. Donald, M.S.
Microbiology Team Leader/Lynne Ensor, Ph.D.

C. CC Block
cc: Field Copy

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- **LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS**

ANDA: 78-208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

A. Microbiology Deficiencies:

1. (b) (4)

2.

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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/s/

Steven P Donald
2/24/2009 11:36:36 AM
MICROBIOLOGIST

Bonnie McNeal
2/26/2009 03:22:22 PM
MICROBIOLOGIST
Checked for correct file and submission link. Both ok.

Lynne Ensor
3/4/2009 07:39:12 AM
MICROBIOLOGIST

Product Quality Microbiology Review

04/20/2009

ANDA: 78-208

Drug Product Name
Proprietary: N/A
Non-proprietary: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%
Drug Product Priority Classification: N/A

Review Number: 4
Dates of Submission(s) Covered by this Review

Letter	Stamp	Consult Sent	Assigned to Reviewer
03/18/2009	03/20/2009	N/A	03/23/09

Submission History (for amendments only)

Submission Date(s)	Microbiology Review #	Review Date(s)
08/27/07	1	08/15/08
10/16/2008	2	08/15/2008
01/13/2009	3	01/28/2009

Applicant/Sponsor
Name: Altaire Pharmaceuticals, Inc.
Address: P. O. Box 849
311 West Lane
Aquebogue, NY 11931
U.S. Agent:
Name: Medvice Consulting, Inc.
Address: 2214 Sanford Dr., Suite B7
Grand Junction, CO 81505
Representative: Mr. Martin Dalsing,
Telephone: 970 243 5490, Fax: 970 243 5501

Name of Reviewer: Steven P. Donald

Conclusion: The submission is **recommended** for approval on the basis of sterility assurance.

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Original Amendment

2. SUBMISSION PROVIDES FOR: Information in response to deficiency letter, dated March 4, 2009, addressing microbiological issues in review #3.

3. MANUFACTURING SITE: Altaire Pharmaceuticals, Inc.
311 West Lane, PO BOX 849 Aquebogue, NY 11931

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Sterile solution, topical, ophthalmic, Pheniramine malate 0.315%, Naphazoline HCl 0.027%, multi-dose, packaged as 0.5 oz. fill in a 15 cc bottle and a 1.0 oz. fill in a 30 cc bottle

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: N/A

B. SUPPORTING/RELATED DOCUMENTS: None

C. REMARKS: None

filename: 78-208a3.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability –
The submission is **recommended** for approval on the basis of sterility assurance.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable –
N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology –
Drug solution is [redacted] (b) (4) [redacted] (b) (4) filled into sterile 15 and 30 ml bottles.

B. Brief Description of Microbiology Deficiencies-
None Identified.

C. Assessment of Risk Due to Microbiology Deficiencies -
No microbiology deficiencies were identified. The applicant demonstrates an adequate level of sterility assurance for the manufacturing process.

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block
Microbiologist / Steven P. Donald, M.S.
Microbiology Team Leader/Lynne Ensor, Ph.D.

C. CC Block
cc: Field Copy

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/s/

Steven P Donald
4/27/2009 07:59:52 AM
MICROBIOLOGIST

Bonnie McNeal
4/29/2009 12:17:25 PM
MICROBIOLOGIST
Checked for correct file and submission link. Both ok.

Lynne Ensor
5/1/2009 07:07:23 AM
MICROBIOLOGIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

PROPRIETARY NAME REVIEW

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	December 5, 2008
To:	William P. Rickman, Director Division of Labeling and Program Support Office of Generic Drugs
Through:	Kellie Taylor, Pharm.D., M.P.H., Team Leader Denise Toyer, Pharm.D., Deputy Director Carol Holquist, R.Ph., Director Division of Medication Error Prevention and Analysis
From:	Cathy A. Miller, M..P.H., Division of Medication Error Prevention and Analysis
Subject:	Proprietary Name, Label, and Labeling Review
Drug Name(s):	(b) (4) (Naphazoline Hydrochloride and Pheniramine Maleate) Ophthalmic Solution 0.02675 % / 0.315 %
Application Type/Number:	ANDA #78-208
Applicant:	Altaire Pharmaceuticals, Inc.
OSE RCM #:	2008-1036

***Note: This review contains proprietary and confidential information that should not be released to the public. ***

CONTENTS

EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment find the proposed name, (b) (4) vulnerable to confusion that could result in medication errors because of its similarity to the currently marketed product, (b) (4) Specifically, we find that orthographic similarities along with many other shared product characteristics such as similar indication of use, single strength availability, dosage form, route of administration and frequency, present a potential for medication error occurring in the usual practicing setting.

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed carton labeling and container label acceptable, consistent with the reference listed product, OpCon-A, and we have no labeling recommendations at this time.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to a request from the Office of Generic Drugs, Division of Labeling and Program Support, to evaluate the proposed proprietary name, (b) (4) along with carton labeling and container labels, for the potential to contribute to medication errors.

1.2 REGULATORY HISTORY

Reference listed drug Opcon-A (Naphazoline Hydrochloride and Pheniramine Maleate), new drug application (NDA 20-065), manufactured by Bausch and Lomb, was approved on June 8, 1994 for temporary relief of itching and redness caused by pollen, ragweed, grass, animal hair and dander and is available without a prescription (over-the-counter). On August 27, 2007, Altaire Pharmaceuticals submitted abbreviated new drug application (ANDA 78-208), along with a request for proprietary name review for (b) (4) On June 25, 2008, the Division of Medication Error Prevention and Analysis was consulted for the proprietary name review of (b) (4)

1.3 PRODUCT INFORMATION

(b) (4) is an ophthalmic eye drop indicated for relieve of minor eye symptoms of itching and redness caused by pollen, ragweed, grass, animal hair, and dander, and will be available without a prescription (over-the-counter). (b) (4) contains Naphazoline Hydrochloride (0.02675 %) and Pheniramine Maleate (0.315 %). (b) (4) should be administered by instilling one or two drops in the affected eye(s) up to four times daily.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by the Division of Medication Error Prevention and Analysis' medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Label and Labeling Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. The Division defines a medication error as any

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/s/

Cathy A Miller
12/5/2008 09:38:01 AM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
12/5/2008 04:32:38 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
12/5/2008 05:28:59 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
12/5/2008 05:31:51 PM
DRUG SAFETY OFFICE REVIEWER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 078208

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

MEDVICE CONSULTING, INC.

Grand Valley Business Plaza - 2214 Sanford Drive, Suite # B
Grand Junction, CO. 81505 US.

Martin Dalsing

(970) 243-5490 Fax (970) 243-5501 Direct Email: Marty@FDApproval.com

78-208

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, ROOM 150
Rockville, MD 20855

March 15, 2006

RE: Abbreviated New Drug Application for: Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

Attention: Document Mail Clerk

To whom it may concern;

This is to notify you of the intention of ***Altaire Pharmaceuticals, Inc.,*** to manufacture, market and distribute the following Generic Drug Product:

Purpose of Submission:	Clearance of Generic Drug Product
Referenced Listed Drug:	Opcon-A™ Eye Drops
Type of Submission:	ANDA
New Drug Product Proprietary Name:	(b) (4) Eye Drops
Establishment Reg #:	2335740
Applicant Name:	Altaire Pharmaceuticals, Inc. Michael S. Sawaya General Counsel P.O. Box 849 311 West Lane Aquebogue, NY 11931
Number of Volumes:	1

RECEIVED
MAR 16 2006
OGD / CDER

MEDVICE CONSULTING, INC.
Drive, Suite # B7

Grand Valley Business Plaza - 2214 Sanford

Grand Junction, CO. 81505 USA

Martin Dalsing
Marty@FDApproval.com

(970) 243-5490 Fax (970) 243-5501 Direct Email:

Letterhead statement: Letterhead from Medvice Consulting, Inc. is being utilized for this cover letter. Reference section XXI of ANDA for authorization letter.

Should additional information be required, the Center for Drug Evaluation and Research should contact the undersigned.

Mr. Martin Dalsing
Official Correspondent and US Consultant for
Altaire Pharmaceuticals, Inc.
Medvice Consulting, Inc.
2214 Sanford Drive, Suite B7
Grand Junction, CO 81505

(970) 243.5490
Fax (970) 243.5501
E-mail: marty@fdapproval.com

Sincerely,

Martin Dalsing

Enclosures

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 78-208 **FIRM NAME:** ALTAIRE PHARMS.

RELATED APPLICATION(S): NA

First Generic Product Received? YES PER MARTY 4/07/06

DRUG NAME: NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE

DOSAGE FORM: SOLUTION/DROPS, 0.027% AND 0.315%

Bio Assignments:		
☒ **BPH**	☐ **BCE**	☒ **Micro Review (No)**
☐ **BST**	☐ **BDI**	

Random Queue: 3
Chem Team Leader: Fan, Jim PM: Rosalyn Adigun Labeling Reviewer: Beverly Wietzman

Letter Date: MARCH 15, 2006	**Received Date:** MARCH 16, 2006
Comments: EC- 2 YES	**On Cards:** YES
Therapeutic Code: 4040400 OPHTHALMIC ADRENERGIC AGENTS	
Archival Format: PAPER	**Sections** I **(356H Sections per EDR Email)**
Review copy: YES Not applicable to electronic sections	E-Media Disposition: NO MEDIA SUBMITTED
Field Copy Certification (Original Signature) YES	
Methods Validation Package (3 copies PAPER archive) **NO** (Required for Non-USP drugs)	
Cover Letter YES	**Table of Contents** YES
PART 3 Combination Product Category (Must be completed for ALL Original Applications)	N Not a Part3 Combo Product Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST **Iain Margand** **Date 5/8/06**	**Recommendation:** ☐ **FILE** ☒ **REFUSE to RECEIVE**
Supervisory Concurrence/Date:	**Date:** 10 MAY 2006
ADDITIONAL COMMENTS REGARDING THE ANDA: **Applicant has failed to provide** [redacted] (b) (4) **drug product (verified with Lynn E.).** **See Refuse to Receive letter for additional deficiencies.** In addition, proposed formulation contains [redacted] (b) (4) RLD does not. does not meet 314.94(a)(9)(iv) or 320.22(b)(1). IM	
Top 200 Drug Product:	

ACCEPTABLE

Sec. I	**Signed and Completed Application Form (356h)** YES (not original signature) (Statement regarding Rx/OTC Status) OTC YES	☐
Sec. II	**Basis for Submission** **NDA# : 20-065** Ref Listed Drug: OPCON-A Firm: BAUSH & LOMB, INC. ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. Wavier Granted:	☒
Sec. III	**Patent Certification** 1. Paragraph: II 2. Expiration of Patent: NA A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? **Exclusivity Statement:** YES No exclusivities	☒
Sec. IV	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same 2. Active ingredients Naphazoline HCl and Pheniramine Maleate 3. Route of administration Ophthalmic 4. Dosage Form Solution/Drops 5. Strength 0.0275% and 0.315%	☒
Sec. V	**Labeling** (Mult Copies N/A for E-Submissions) No electronic submission 1. 4 copies of draft (each strength and container) or 12 copies of FPL Need three more copies of package insert draft. 2. 1 RLD label and 1 RLD container label Y 3. 1 side by side labeling comparison with all differences annotated and explained no annotations 4. Was a proprietary name request submitted? Yes (If yes, send email to Labeling Rvwr indicating such.)	☐
Sec. VI	**Bioavailability/Bioequivalence** **1. Financial Certification** (Form FDA 3454) **and Disclosure Statement** (Form 3455) NO **2. Request for Waiver of In-Vivo Study(ies): YES PAGE 42 need to cite 21 CFR 320.22(b)(1)** **3. Formulation data same?** (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals) Same active and inactives with allowable changes **4. Lot Numbers of Products used in BE Study(ies):** N/A **5. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐
Study Type	**IN-VIVO PK STUDY(IES)** (i.e., fasting/fed/sprinkle) NA – no bio studies done. a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted: NO MEDIA SUBMITTED c. In-Vitro Dissolution: NO	☐

Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** NO a. <u>In-Vivo PK Study</u> 1. Study(ies) meet BE Criteria (90% CI or 80-125, Cmax, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted b. <u>Adhesion Study</u> c. <u>Skin Irritation/Sensitization Study</u>	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO a. <u>Solutions</u> (Q1/Q2 sameness): 1. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) b. <u>Suspensions</u> (Q1/Q2 sameness): 1. In-Vivo PK Study a. Study(ies) meets BE Criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted 2. In-Vivo BE Study with Clinical EndPoints a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted 3. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO a. Pilot Study (determination of ED50) b. Pivotal Study (study meets BE criteria 90%CI or 80-125)	☐
Sec. VII	**Components and Composition Statements** 1. Unit composition and batch formulation Y 2. Inactive ingredients as appropriate Inactive ingredients are acceptable per IIG and COMIS. Changes are allowed under 21CFR 314.94(a)(9)(iv).	☒

Sec. VIII	**Raw Materials Controls** 1. **Active Ingredients** a. Addresses of bulk manufacturers Y no contact person Naphazoline – DMF (b) (4) b. Type II DMF authorization letters or synthesis Pheniramine – DMF c. COA(s) specifications and test results from drug substance mfgr(s) COA not from mfr d. Applicant certificate of analysis Y e. Testing specifications and data from drug product manufacturer(s) Y f. Spectra and chromatograms for reference standards and test samples Y g. CFN numbers 2. **Inactive Ingredients** a. Source of inactive ingredients identified pg. 47 b. Testing specifications (including identification and characterization) Y c. Suppliers' COA (specifications and test results) Y d. Applicant certificate of analysis Y	☐
Sec.IX	**Description of Manufacturing Facility** 1. Full Address(es)of the Facility(ies) YES 2. CGMP Certification: YES – does not cite 21 CFR 210 and 211 3. CFN numbers	☐
Sec. X	**Outside Firms Including Contract Testing Laboratories** 1. Full Address Y 2. Functions Y 3. CGMP Certification/GLP Do not cite 21 CFR 210 and 211 4. CFN numbers	☐
Sec. XI	**Manufacturing and Processing Instructions** 1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) No 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) 3.If sterile product: Aseptic fill / Terminal sterilization (b) (4) 4. Filter validation (if aseptic fill) no, per Lynn E. 5. Reprocessing Statement needs to be revised	☐
Sec. XII	**In-Process Controls** 1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation 2. In-process Controls - Specifications and data Y Ty: (b) (4) Ay: Packaged: 15 mL (b) (4) 30 mL (b) (4)	☐
Sec. XIII	**Container** 1. Summary of Container/Closure System (if new resin, provide data) pg. 417 2. Components Specification and Test Data (Type III DMF References) Testing specs given, but no data. Need to provide DMF letters for (b) (4). 3. Packaging Configuration and Sizes 15 mL and 30 mL plastic bottles 4. Container/Closure Testing no 5. Source of supply and suppliers address pg. 419	☐

Sec. XIV	**Controls for the Finished Dosage Form** 1. Testing Specifications and Data Y 2. Certificate of Analysis for Finished Dosage Form no lot numbers on COA's (pgs. 551 & 552)	☐
Sec. XV	**Stability of Finished Dosage Form** 1. Protocol submitted Y 2. Post Approval Commitments not provided 3. Expiration Dating Period 2 years 4. Stability Data Submitted a. 3 month accelerated stability data No, provided 36 month RT b. Batch numbers on stability records the same as the test batch lot# 03284 **provided accelerated stability information, but lot # is not the same as exhibit batch**	☐
Sec. XVI	**Samples** - Statement of Availability and Identification of: 1. Drug Substance Y 2. Finished Dosage Form 15 mL only 3. Same lot numbers no lot numbers given	☐
Sec. XVII	**Environmental Impact Analysis Statement**	☒
Sec. XVIII	**GDEA (Generic Drug Enforcement Act)/Other:** 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) YES 2. Debarment Certification (original signature): YES 3. List of Convictions statement (original signature) YES 4. Field Copy Certification (original signature) need to cite 21 CFR 314.94(d)(5)	☐

OGD Template Revised 04/01/2004 /T.Hinchliffe

ANDA 78-208

MAY 11 2006

Medvice Consulting, Inc.
U.S. Agent for: Altaire Pharmaceuticals, Inc.
Attention: Martin Dalsing
2214 Sanford Drive, Suite B7
Grand Junction, CO 81505

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated March 15, 2006 submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution, 0.027% and 0.315%, 15 mL and 30 mL containers.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to receive this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

You have failed to provide (b)(4) data as part of your manufacturing and processing instructions. (b)(4) (b)(4) is a necessary requirement for any products which are (b)(4). This data is required to be finished and complete upon submission of the application to the office.

Generally, a drug product intended for ophthalmic use shall contain the same inactive ingredients and in the same concentration as the reference listed drug. An applicant may only seek approval of an ophthalmic product if it differs from the reference listed drug in preservative, buffer, substance to adjust tonicity, or thickening agent [21 CFR 314.94(a)(9)(iv)]. Your formulation involves qualitative changes, (b)(4) (b)(4), which are not allowable changes for an ophthalmic product.

> Your proposed formulation does not meet the bioequivalence waiver requirements under 21 CFR 320.22(b)(1). To be eligible for a waiver of evidence of *in vivo* bioequivalence under 21 CFR 320.22(b)(1), your proposed product must contain the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full new drug application.

Thus, it will not be received as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

In addition, please provide the following:

Please cite Section 505(j) of the Federal Food, Drug and Cosmetic Act in your cover letter.

Pursuant to CFR 314.94(d)(5), please provide certification to state that a "true copy" of the technical sections of the application has been submitted to the appropriate district office.

All ANDAs submitted after June 8, 2003, are required to provide a minimum of the proposed package insert in electronic format. Please consult FR Vol. 68 No. 238, pp. 69009-69020, December 11, 2003, for additional information.

Please provide an additional three copies of your proposed package insert.

Please provide a side-by-side comparison of the proposed package labeling and proposed package insert with the reference listed drug with any differences annotated and explained.

Please provide a form 356h with original signature.

Please provide a contact person for the Active Pharmaceutical Ingredient (API) manufacturers.

The Certificate of Analysis for the API Naphazoline Hydrochloride is from (b)(4), though the manufacturer is (b)(4). Please clarify if (b)(4) is the U.S. Agent for (b)(4) and if so, please provide a letter of authorization for (b)(4) to act as the U.S. Agent for (b)(4).

The Certificate of Analysis for the API Pheniramine Maleate is from (b)(4), though the manufacturer is (b)(4). Please clarify if (b)(4) is the U.S. Agent for (b)(4) and if so, please provide a letter of authorization for (b)(4) to act as the U.S. Agent for (b)(4).

Please provide a cGMP from the drug product manufacturer that cites 21 CFR 210 and 211.

Please provide a cGMP/cGLP from [redacted] that cite 21 CFR 210 and 211.

Please provide a description of the manufacturing process.

Please provide a Reprocessing Statement for the production of the drug product under 21 CFR 211.115.

Please provide the theoretical fill amounts for the 15 mL and 30 mL container sizes in the exhibit batch.

Please provide a DMF Type III letter of authorization from [redacted] for the [redacted].

We note you have provided component test specifications for the proposed bottles, dropper tip and tip closure. Please provide the results of these tests (section XIII, no. 2 on the checklist).

Please provide container/closure testing results (section XIII, no. 4 on the checklist).

Please provide lot numbers for 15 mL and 30 mL Certificates of Analysis located on pages 551 and 552 of the application in the Controls for the Finished Dosage Form section.

Please provide Post-Approval Stability Commitments for the finished drug product.

Please provide lot numbers for the drug substances and drug products in your Samples Availability Statement and please include the 30 mL finished drug product container size.

Upon receipt of this communication, you may either amend your application to correct the deficiencies or withdraw your application under 21 CFR 314.99. If you have any questions please call:

Iain Margand
Project Manager
(301) 827-5862

Sincerely yours,

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 78-208
cc: DUP/Jackets
HFD-600/Division File
Field Copy
HFD-610/G. Davis
HFD-92

Endorsement: HFD-615/MShimer, Chief, RSB date 11 May 06
HFD-615/IMargand, CSO date 5/11/06
Word File V:\Firmsam\Altaire\Ltrs&rev\78208.rtf
F/T 5/8/06
ANDA Refuse to Receive!

MEDVICE CONSULTING, INC. MCI Inc.
Grand Valley Business Plaza - 2214 Sanford Drive, Suite # B7
Grand Junction, CO. 81505 USA

Martin Dalsing
☎ (970) 243-5490 Fax (970) 243-5501 Direct Email: Marty@FDApproval.com

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, ROOM 150
Rockville, MD 20855

June 26th, 2006

N/AC

RE: ANDA 78-208
Abbreviated New Drug Application for: Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

Attention: Document Mail Clerk

To whom it may concern;

Please allow the following (including attachments) to serve as Altaire's response the comments issued on or about May 19, 2006 referable to ANDA no. 78-208, for Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution, 0.027% and 0.315%, 15 mL and 30 mL containers.

We expect that said response appropriately completes our application, addresses the comments and issues, and respectfully request that the critical technical review commence.

This ANDA supplement submission is being submitted in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act.

Should additional information be required, the Center for Drug Evaluation and Research should contact the undersigned.

Mr. Martin Dalsing
Official Correspondent and US Consultant for
Altaire Pharmaceuticals, Inc.

Sincerely,

Martin Dalsing

RECEIVED
JUN 29 2006
OGD / CDER

Enclosures

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-208

CERTIFIED MAIL-RETURN RECEIPT REQUESTED

Medvice Consulting, Inc.
U.S. Agent for: Altaire Pharmaceuticals, Inc.
Attention: Martin Dalsing
2214 Sanford Drive, Suite B7
Grand Junction, CO 81505

Dear Sir:

This letter is in reference to your Abbreviated New Drug Application (ANDA) dated March 15, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution, 0.027% and 0.315%, 15 mL and 30 mL containers.

We sent you "Refuse-to-Receive" letter dated June 29, 2006, which detailed the deficiencies identified during our preliminary review. We are unaware of any subsequent correspondence from you that sought to either address the deficiencies or advise us of your intent to file an amendment.

Absent evidence of interest on the part of an applicant over such a prolonged time can be considered as a request for withdrawal pursuant to the authority cited in Section 314.120 of the regulations.

Alternatively, if you do not intend to immediately pursue approval of this application you may request withdrawal in accord with Section 314.65 of the regulations. If you do elect to request withdrawal, it will not preclude a future refiling.

If we do not receive a definitive reply from you within 10 days of receipt of this letter, in which you request withdrawal or provide substantive amendment to the application that seek to address the deficiencies noted, we will initiate action to withdraw this application.

If you have further questions you may contact Saundra T. Middleton, Project Manager, Regulatory Support Branch, at (301) 827-0498.

Please send all correspondence to the following address:

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Saundra Middleton
3/8/2007 12:08:03 PM
Signing for Wm Peter Rickman

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 78-208 **FIRM NAME**: ALTAIRE PHARMS.

RELATED APPLICATION(S): NA

First Generic Product Received? YES PER MARTY 4/07/06

DRUG NAME: NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE

DOSAGE FORM: SOLUTION/DROPS, 0.027% AND 0.315%

Bio Assignments:		Micro Review (No)
☒ BPH	☐ BCE	
☐ BST	☐ BDI	

Random Queue: 3
Chem Team Leader: Fan, Jim PM: Rosalyn Adigun Labeling Reviewer: Beverly Wietzman

Letter Date: MARCH 15, 2006 **Received Date**: MARCH 16, 2006

Comments: EC- 2 YES **On Cards:** YES
Therapeutic Code: 4040400 OPHTHALMIC ADRENERGIC AGENTS

Archival Format: PAPER **Sections** I **(356H Sections per EDR Email)**
Review copy: YES E-Media Disposition: NO MEDIA SUBMITTED
Not applicable to electronic sections
Field Copy Certification (Original Signature) YES

Methods Validation Package (3 copies PAPER archive) **NO**
(Required for Non-USP drugs)

Cover Letter YES | **Table of Contents** YES

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Iain Margand

Date 3/22/07

Recommendation:

☐ **FILE** ☒ **REFUSE to RECEIVE**

Supervisory Concurrence/Date: ____ **Date:** ____

ADDITIONAL COMMENTS REGARDING THE ANDA:
Applicant has failed to provide (b) (4) **for the** (b) (4) **drug product (verified with Lynn E.).**
See Refuse to Receive letter for additional deficiencies.
3/22/07Applicant submitted response to deficiencies in RTR letter. Applicant states the drug product contains pH adjusters based on the PDR, not on labeling. I am unable to verify the use of pH adjusters in the RLD. Also of note, this ANDA, 78-208 is the (b) (4) **the application has been submitted to OGD by this applicant. The application for generic Opcon-A had been submitted under** (b) (4) .

Top 200 Drug Product:

ACCEPTABLE

Sec. I	**Signed and Completed Application Form (356h)** YES (not original signature) (Statement regarding Rx/OTC Status) OTC YES	☐
Sec. II	**Basis for Submission** **NDA# : 20-065** Ref Listed Drug: OPCON-A Firm: BAUSH & LOMB, INC. ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. Wavier Granted:	☒
Sec. III	**Patent Certification** 1. Paragraph: II 2. Expiration of Patent: NA A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? **Exclusivity Statement:** YES No exclusivities	☒
Sec. IV	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same 2. Active ingredients Naphazoline HCl and Pheniramine Maleate 3. Route of administration Ophthalmic 4. Dosage Form Solution/Drops 5. Strength 0.0275% and 0.315%	☒
Sec. V	**Labeling** (Mult Copies N/A for E-Submissions) No electronic submission 1. 4 copies of draft (each strength and container) or 12 copies of FPL Need three more copies of package insert draft. 2. 1 RLD label and 1 RLD container label Y 3. 1 side by side labeling comparison with all differences annotated and explained no annotations 4. Was a proprietary name request submitted? Yes (If yes, send email to Labeling Rvwr indicating such.)	☐
Sec. VI	**Bioavailability/Bioequivalence** **1. Financial Certification** (Form FDA 3454) **and Disclosure Statement** (Form 3455) NO **2. Request for Waiver of In-Vivo Study(ies): YES PAGE 42 need to cite 21 CFR 320.22(b)(1)** **3. Formulation data same?** (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals) Same active and inactives with allowable changes **4. Lot Numbers of Products used in BE Study(ies):** N/A **5. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☐
Study Type	**IN-VIVO PK STUDY(IES)** (i.e., fasting/fed/sprinkle) NA – no bio studies done. a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted: NO MEDIA SUBMITTED c. In-Vitro Dissolution: NO	☐

Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** NO a. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI or 80-125, Cmax, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted b. Adhesion Study c. Skin Irritation/Sensitization Study	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO a. Solutions (Q1/Q2 sameness): 1. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) b. Suspensions (Q1/Q2 sameness): 1. In-Vivo PK Study a. Study(ies) meets BE Criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted 2. In-Vivo BE Study with Clinical EndPoints a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted 3. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO a. Pilot Study (determination of ED50) b. Pivotal Study (study meets BE criteria 90%CI or 80-125)	☐
Sec. VII	**Components and Composition Statements** 1. Unit composition and batch formulation Y 2. Inactive ingredients as appropriate Inactive ingredients are acceptable per IIG and COMIS. Changes are allowed under 21CFR 314.94(a)(9)(iv).	☒

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Sec. X	**Outside Firms Including Contract Testing Laboratories** 1. Full Address Y 2. Functions Y 3. CGMP Certification/GLP Do not cite 21 CFR 210 and 211 4. CFN numbers	☐
Sec. XI	**Manufacturing and Processing Instructions** 1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) No 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) 3.If sterile product: Aseptic fill / Terminal sterilization (b) (4) 4. Filter validation (if aseptic fill) no, per Lynn E. 5. Reprocessing Statement needs to be revised	☐
Sec. XII	**In-Process Controls** 1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation 2. In-process Controls - Specifications and data Y Ty: (b) (4) Ay: Packaged: 15 mL (b) (4) 30 mL (b) (4)	☐
Sec. XIII	**Container** 1. Summary of Container/Closure System (if new resin, provide data) pg. 417 2. Components Specification and Test Data (Type III DMF References) Testing specs given, but no data. Need to provide DMF letters for (b) (4) 3. Packaging Configuration and Sizes 15 mL and 30 mL plastic bottles 4. Container/Closure Testing no 5. Source of supply and suppliers address pg. 419	☐

Sec. XIV	**Controls for the Finished Dosage Form** 1. Testing Specifications and Data Y 2. Certificate of Analysis for Finished Dosage Form no lot numbers on COA's (pgs. 551 & 552)	☐
Sec. XV	**Stability of Finished Dosage Form** 1. Protocol submitted Y 2. Post Approval Commitments not provided 3. Expiration Dating Period 2 years 4. Stability Data Submitted a. 3 month accelerated stability data No, provided 36 month RT b. Batch numbers on stability records the same as the test batch lot# 03284 **provided accelerated stability information, but lot # is not the same as exhibit batch**	☐
Sec. XVI	**Samples** - Statement of Availability and Identification of: 1. Drug Substance Y 2. Finished Dosage Form 15 mL only 3. Same lot numbers no lot numbers given	☐
Sec. XVII	**Environmental Impact Analysis Statement**	☒
Sec. XVIII	**GDEA (Generic Drug Enforcement Act)/Other**: 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) YES 2. Debarment Certification (original signature): YES 3. List of Convictions statement (original signature) YES 4. Field Copy Certification (original signature) need to cite 21 CFR 314.94(d)(5)	☐

OGD Template Revised 04/01/2004 /T.Hinchliffe

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

/s/

Martin Shimer

3/23/2007 12:37:29 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-208

Medvice Consulting, Inc.
U.S. Agent for: Altaire Pharmaceuticals, Inc.
Attention: Martin Dalsing
2214 Sanford Drive, Suite B7
Grand Junction, CO 81505

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated March 15, 2006 submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Naphazoline Hydrochloride and Pheniramine Maleate Ophthalmic Solution, 0.027% and 0.315%, 15 mL and 30 mL containers.

Reference is made to the "Refuse to Receive" letter dated May 11, 2006 and to your amendment dated June 26, 2006.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to receive this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

Generally, a drug product intended for ophthalmic use shall contain the same inactive ingredients and in the same concentration as the reference listed drug. An applicant may only seek approval of an ophthalmic product if it differs from the reference listed drug in preservative, buffer, substance to adjust tonicity, or thickening agent [21 CFR 314.94(a)(9)(iv)]. Your formulation involves qualitative changes, (b) (4) which are not allowable changes for an ophthalmic product.

Your proposed formulation does not meet the bioequivalence waiver requirements under 21 CFR 320.22(b)(1). To be eligible for a waiver of evidence of *in vivo* bioequivalence under 21 CFR 320.22(b)(1), your proposed product must contain the same active and inactive ingredients in the same

concentration as a drug product that is the subject of an approved full new drug application.

Thus, it will not be received as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

We note the "Refuse to Receive" letter dated August 20, 2004 for ANDA (b) (4) in which the application was refused due to the drug product not being "qualitatively and quantitatively ent to the reference listed drug". The formulation in ANDA (b) (4) contains the same components as in ANDA 78-208.

Upon receipt of this communication, you may either amend your application to correct the deficiencies or withdraw your application under 21 CFR 314.99. If you have any questions please call:

Iain Margand
Project Manager
(301)827-5835

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Martin Shimer
3/23/2007 12:54:38 PM
Signing for Wm Peter Rickman

MEDVICE CONSULTING, INC.

Grand Valley Business Plaza - 2214 Sanford Drive, Suite # B7
Grand Junction, CO. 81505 USA

Martin Dalsing

(970) 243-5490 Fax (970) 243-5501 Direct Email: Marty@FDApproval.com

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, ROOM 150
Rockville, MD 20855

May 6, 2007

MC

RE: Amendment Abbreviated New Drug Application ANDA 78-208 for: Pheniramine Maleate 0.315% and Naphazoline HCI 0.027% Ophthalmic Solution

Attention: Document Mail Clerk

To whom it may concern;

This is an amendment to ANDA 78-208 an unapproved abbreviated application submitted by ***Altaire Pharmaceuticals, Inc.*** to manufacture, market and distribute the following Generic Drug Product:

Purpose of Submission: Clearance of Generic Drug Product

Referenced Listed Drug: Opcon-A™ Eye Drops

Type of Submission: ANDA

New Drug Product Proprietary Name: (b) (4) Eye Drops

Establishment Reg #: 2335740

Altaire Pharmaceuticals, Inc.

Michael S. Sawaya
General Counsel
P.O. Box 849
311 West Lane
Aquebogue, NY 11931

RECEIVED
MAY 09 2007
OGD

MEDVICE CONSULTING, INC.

Grand Valley Business Plaza - 2214 Sanford Drive, Suite # B7
Grand Junction, CO. 81505 USA

Martin Dalsing

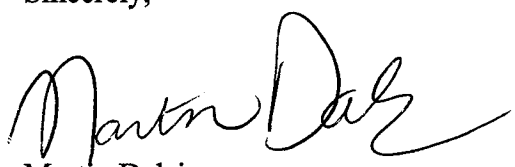
(970) 243-5490 Fax (970) 243-5501 Direct Email: Marty@FDApproval.com

This amendment should address open issues as noted by Iain Margand, Project Manager via letter. We are confident that the enclosed information is sufficient to accept and review ANDA 78-208. Should additional information be required, the Center for Drug Evaluation and Research should contact the undersigned.

Mr. Martin Dalsing
Official Correspondent and US Consultant for
Altaire Pharmaceuticals, Inc.
Medvice Consulting, Inc.
2214 Sanford Drive, Suite B7
Grand Junction, CO 81505

(970) 243.5490
Fax (970) 243.5501
E-mail: marty@fdapproval.com

Sincerely,



Martin Dalsing

Enclosures

MEDVICE CONSULTING, INC.

Martin Dalsing

Grand Valley Business Plaza - 2214 Sanford Drive, Suite # B7
Grand Junction, CO. 81505 USA
(970) 243-6490 Fax (970) 243-5501 Direct Email: Marty@FDApproval.com

Office of Generic Drugs
CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

August 27, 2007

MC

RE: Amendment for Abbreviated New Drug Application ANDA 78-208: Pheniramin Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

Attention: Document Mail Clerk

To Whom It May Concern:

This is an amendment to ANDA 78-208 and needs to be forwarded to Ian Margand.

Sincerely,

Martin Dalsing,
Medvice Consulting, Inc.

enclosures

(b) (4)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-208

Medvice Consulting, Inc.
U.S. Agent for: Altaire Pharmaceuticals, Inc.
Attention: Martin Dalsing
2214 Sanford Drive, Suite B7
Grand Junction, CO 81505

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to our "Refuse to Receive" letters dated May 11, 2006 and March 23, 2007 and your amendments dated June 26, 2006, May 6, 2007 and August 27, 2007 and your correspondence dated September 21, 2007.

NAME OF DRUG: Naphazoline Hydrochloride and Pheniramine Maleate
Ophthalmic Solution, 0.027% and 0.315%,
15 mL and 30 mL containers

DATE OF APPLICATION: March 15, 2006

DATE (RECEIVED) ACCEPTABLE FOR FILING: August 28, 2007

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Rosalyn Adigun
Project Manager
301-827-5754

Sincerely yours,

{See appended electronic signature page}

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Martin Shimer
10/26/2007 08:16:55 AM
Signing for Wm Peter Rickman

ANDA CHECKLIST
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION

ANDA Nbr: 78-208 **FIRM NAME**: ALTAIRE PHARMS.

RELATED APPLICATION(S): NA

First Generic Product Received? YES PER MARTY 4/07/06

DRUG NAME: NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE

DOSAGE FORM: SOLUTION/DROPS, 0.027% AND 0.315%

Bio Assignments:		
☒ **BPH**	☐ **BCE**	☒ **Micro Review (No)**
☐ **BST**	☐ **BDI**	

Random Queue: 3

Chem Team Leader: Fan, Jim PM: Rosalyn Adigun Labeling Reviewer: Beverly Wietzman

Letter Date: MARCH 15, 2006 **Received Date**: MARCH 16, 2006

Comments: EC- 2 YES **On Cards:** YES

Therapeutic Code: 4040400 OPHTHALMIC ADRENERGIC AGENTS

Archival Format: PAPER **Sections** I **(356H Sections per EDR Email)**

Review copy: YES E-Media Disposition: NO MEDIA SUBMITTED

Not applicable to electronic sections

Field Copy Certification (Original Signature) YES

Methods Validation Package (3 copies PAPER archive) **NO**
(Required for Non-USP drugs)

Cover Letter YES | **Table of Contents** YES

PART 3 Combination Product Category N Not a Part3 Combo Product

(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Iain Margand	**Recommendation:**
Date 10/1/07	☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: _____	**Date:** _____

ADDITIONAL COMMENTS REGARDING THE ANDA:

Applicant has (b) (4) for the (b) (4) drug product (verified with Lynn E.).

See Refuse to Receive letter for additional deficiencies.

3/22/07Applicant submitted response to deficiencies in RTR letter. Applicant states (b) (4)

7/27/07: Applicant has provided additional amendment dated 5/6/07. The firm has (b) (4) (b) (4) the formulation. The only other change in the formulation from the original submission is the (b) (4)

S/W Dr. Fan in regards to the revised formulation. Dr. Fan would like to see the firm produce a new batch of the proposed drug product to demonstrate the product will meet the intended (b) (4) The firm needs to show the new formulation is equivalent to the initial proposed formula. These concerns were relayed to Altaire Pharmacutical in a telephone conversation 8/9/07.

9/7/07: Received an amendment to application which includes an executed batch record using the revised formulation as well as COA for the finished product which demonstrates the exhibit product meets the (b) (4) set forth by the drug product manufacturer, (b) (4). Still have not received information pertaining to API contact person, LOA for U.S. Agent for API, DMF LOA from (b) (4) DMF LOA from (b) (4). Sent e-mail to Mr. Dalsing with request for missing information.

9/21/07: Requested information faxed to office. U.S. Agent LOA and LOA from (b) (4) still pending and will be provided as soon as available. Application will be accepted for filing.

(b) (4)

Contact: Martin Dalsing 970-243-5501

Top 200 Drug Product:

ACCEPTABLE

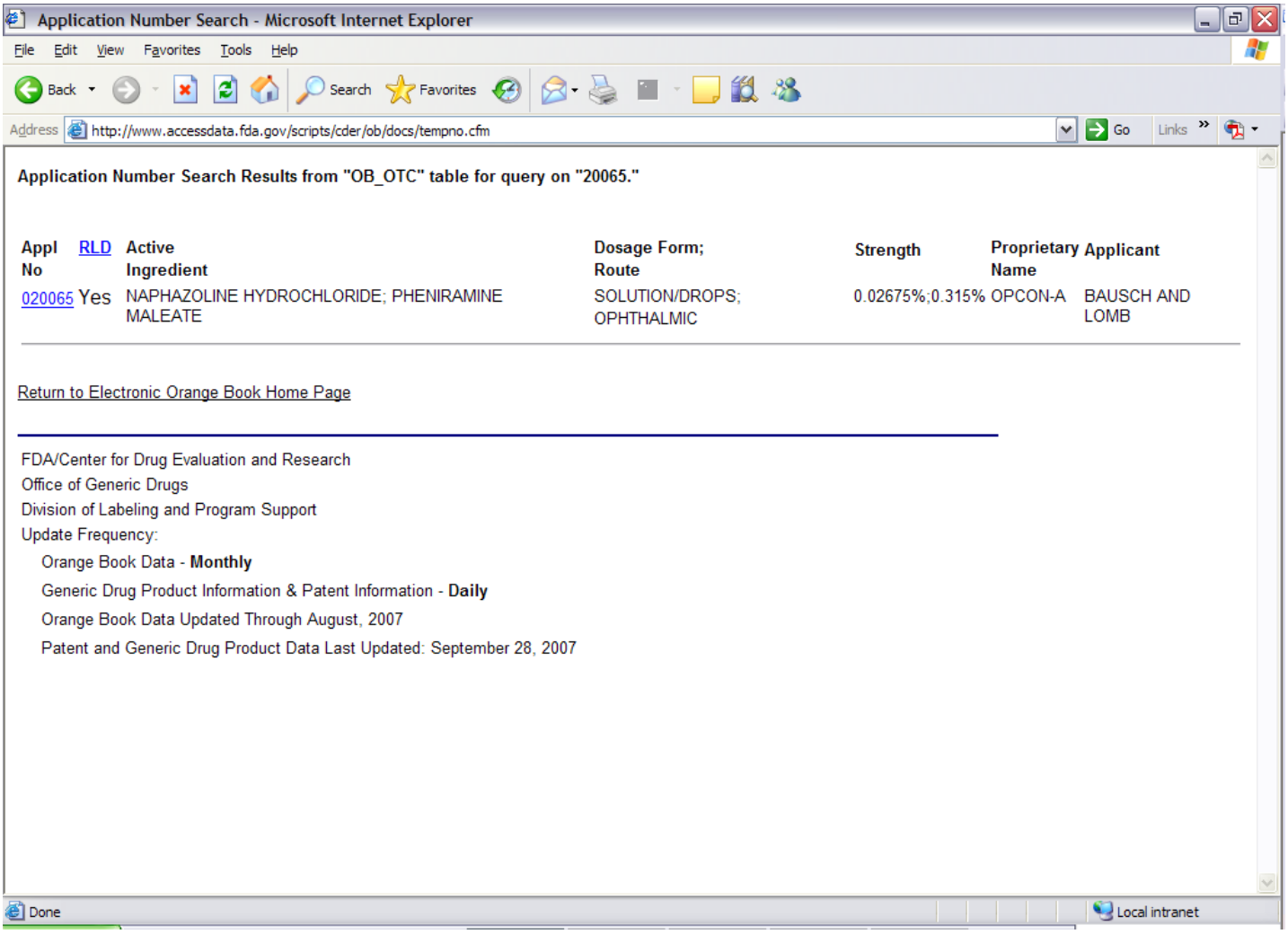
Sec. I	**Signed and Completed Application Form (356h)** YES (not original signature) (Statement regarding Rx/OTC Status) OTC YES	☐
Sec. II	**Basis for Submission** **NDA# : 20-065** Ref Listed Drug: OPCON-A Firm: BAUSH & LOMB, INC. ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route, active ingredient) For products subject to PREA a wavier request must be granted prior to approval of ANDA. Wavier Granted:	☒
Sec. III	**Patent Certification** 1. Paragraph: II 2. Expiration of Patent: NA A. Pediatric Exclusivity Submitted? B. Pediatric Exclusivity Tracking System checked? **Exclusivity Statement:** YES No exclusivities	☒
Sec. IV	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same 2. Active ingredients Naphazoline HCl and Pheniramine Maleate 3. Route of administration Ophthalmic 4. Dosage Form Solution/Drops 5. Strength 0.0275% and 0.315%	☒
Sec. V	**Labeling** (Mult Copies N/A for E-Submissions) No electronic submission 1. 4 copies of draft (each strength and container) or 12 copies of FPL (se amendment9/26/06) 2. 1 RLD label and 1 RLD container label Y 3. 1 side by side labeling comparison with all differences annotated and explained 4. Was a proprietary name request submitted? Yes (If yes, send email to Labeling Rvwr indicating such.)	☒
Sec. VI	**Bioavailability/Bioequivalence** **1. Financial Certification** (Form FDA 3454) **and Disclosure Statement** (Form 3455) NO **2. Request for Waiver of In-Vivo Study(ies): YES PAGE 42** **3. Formulation data same?** (Comparison of all Strengths) (Ophthalmics, Otics, Topicals Perenterals) Same active and inactives with allowable changes **4. Lot Numbers of Products used in BE Study(ies):** N/A **5. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☒
Study Type	**IN-VIVO PK STUDY(IES)** (i.e., fasting/fed/sprinkle) NA – no bio studies done. a. Study(ies) meets BE criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted: NO MEDIA SUBMITTED c. In-Vitro Dissolution: NO	☐

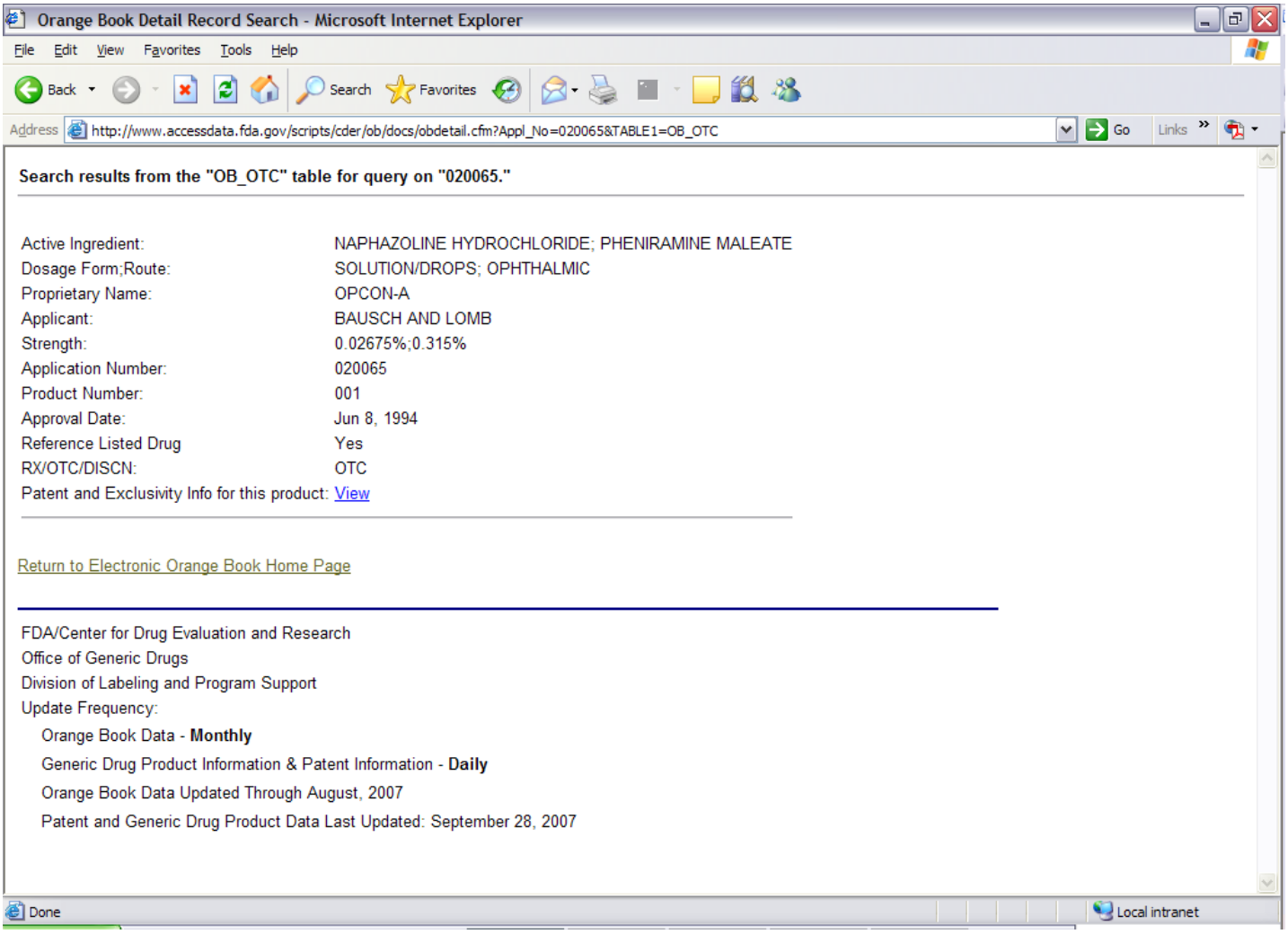
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted	☐
Study Type	**TRANSDERMAL DELIVERY SYSTEMS** NO a. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI or 80-125, Cmax, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted b. Adhesion Study c. Skin Irritation/Sensitization Study	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO a. Solutions (Q1/Q2 sameness): 1. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) b. Suspensions (Q1/Q2 sameness): 1. In-Vivo PK Study a. Study(ies) meets BE Criteria (90% CI or 80-125, Cmax, AUC) b. EDR Email: Data Files Submitted 2. In-Vivo BE Study with Clinical EndPoints a. Properly defined BE endpoints (eval. by Clinical Team) b. Summary results meet BE criteria (90% CI within +/- 20% or 80-120) c. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) d. EDR Email: Data Files Submitted 3. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO a. Pilot Study (determination of ED50) b. Pivotal Study (study meets BE criteria 90%CI or 80-125)	☐
Sec. VII	**Components and Composition Statements** 1. Unit composition and batch formulation Y 2. Inactive ingredients as appropriate — Inactive ingredients are acceptable per IIG and COMIS. Changes are allowed under 21CFR 314.94(a)(9)(iv).	☒

Sec. VIII	**Raw Materials Controls** 1. **Active Ingredients** a. Addresses of bulk manufacturers Y Naphazoline – DMF# (b) (4) b. Type II DMF authorization letters or synthesis Pheniramine – DMF# (b) (4) c. COA(s) specifications and test results from drug substance mfgr(s) COA not from mfr d. Applicant certificate of analysis Y e. Testing specifications and data from drug product manufacturer(s) Y f. Spectra and chromatograms for reference standards and test samples Y g. CFN numbers 2. **Inactive Ingredients** a. Source of inactive ingredients identified pg. 47 b. Testing specifications (including identification and characterization) Y c. Suppliers' COA (specifications and test results) Y d. Applicant certificate of analysis Y	☒
Sec.IX	**Description of Manufacturing Facility** 1. Full Address(es)of the Facility(ies) YES 2. CGMP Certification: YES 3. CFN numbers	☒
Sec. X	**Outside Firms Including Contract Testing Laboratories** 1. Full Address Y 2. Functions Y 3. CGMP Certification/GLP Y 4. CFN numbers	☒
Sec. XI	**Manufacturing and Processing Instructions** 1. Description of the Manufacturing Process (including Microbiological Validation, if Appropriate) No 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) 3.If sterile product: Aseptic fill / Terminal sterilization (b) (4) 4. Filter validation (if aseptic fill) (b) (4) 5. Reprocessing Statement	☒
Sec. XII	**In-Process Controls** 1. Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation 2. In-process Controls - Specifications and data Y Ty: (b) (4) (see 8/27/07 amendment) Ay 15 mL : (b) (4)	☒
Sec. XIII	**Container** 1. Summary of Container/Closure System (if new resin, provide data) pg. 417 2. Components Specification and Test Data (Type III DMF References) See 6/26/06 amendment 3. Packaging Configuration and Sizes 15 mL and 30 mL plastic bottles 4. Container/Closure Testing 5. Source of supply and suppliers address pg. 419	☒

Sec. XIV	**Controls for the Finished Dosage Form** 1. Testing Specifications and Data Y 2. Certificate of Analysis for Finished Dosage Form Y (see 6/26/07 amendment)	☒
Sec. XV	**Stability of Finished Dosage Form** 1. Protocol submitted Y 2. Post Approval Commitments 3. Expiration Dating Period 2 years 4. Stability Data Submitted a. 3 month accelerated stability data No, provided 36 month RT b. Batch numbers on stability records the same as the test batch lot# 03284	☒
Sec. XVI	**Samples** - Statement of Availability and Identification of: (see 6/26/07 amendment) 1. Drug Substance Y 2. Finished Dosage Form 3. Same lot numbers	☒
Sec. XVII	**Environmental Impact Analysis Statement**	☒
Sec. XVIII	**GDEA (Generic Drug Enforcement Act)/Other**: 1. Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) YES 2. Debarment Certification (original signature): YES 3. List of Convictions statement (original signature) YES 4. Field Copy Certification (original signature)	☐

OGD Template Revised 04/01/2004 /T.Hinchliffe


Application Number Search - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back Search Favorites
Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/tempno.cfm
Go Links
Application Number Search Results from "OB_OTC" table for query on "20065."
Appl No
RLD
Active Ingredient
Dosage Form; Route
Strength
Proprietary Name
Applicant
020065 Yes NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE SOLUTION/DROPS; OPHTHALMIC 0.02675%;0.315% OPCON-A BAUSCH AND LOMB
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through August, 2007
Patent and Generic Drug Product Data Last Updated: September 28, 2007
Done
Local intranet


Orange Book Detail Record Search - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back Search Favorites
Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/obdetail.cfm?Appl_No=020065&TABLE1=OB_OTC
Go Links
Search results from the "OB_OTC" table for query on "020065."
Active Ingredient: NAPHAZOLINE HYDROCHLORIDE; PHENIRAMINE MALEATE
Dosage Form;Route: SOLUTION/DROPS; OPHTHALMIC
Proprietary Name: OPCON-A
Applicant: BAUSCH AND LOMB
Strength: 0.02675%;0.315%
Application Number: 020065
Product Number: 001
Approval Date: Jun 8, 1994
Reference Listed Drug Yes
RX/OTC/DISCN: OTC
Patent and Exclusivity Info for this product: View
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through August, 2007
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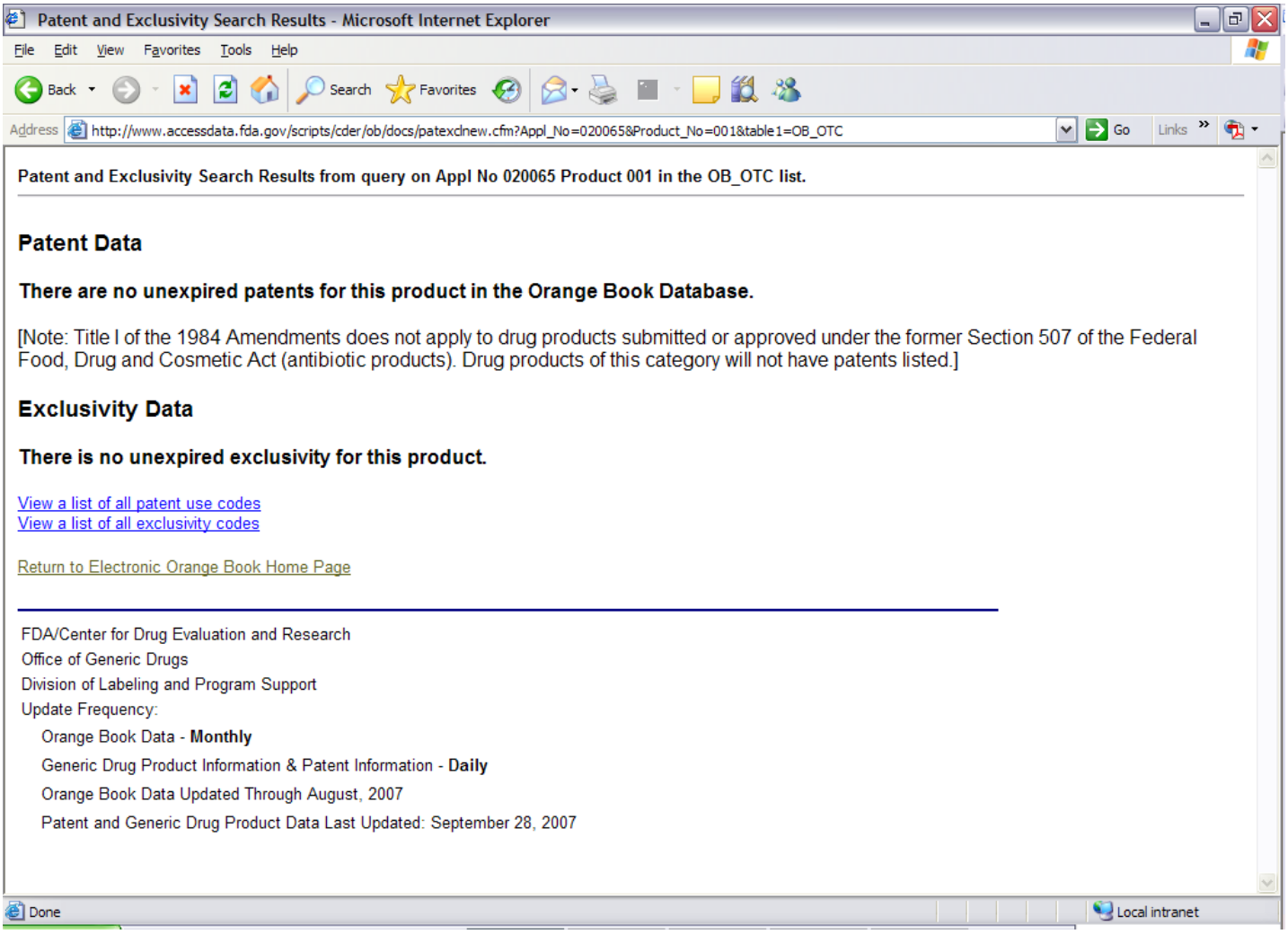
Patent and Exclusivity Search Results - Microsoft Internet Explorer
File Edit View Favorites Tools Help
Back Search Favorites
Address http://www.accessdata.fda.gov/scripts/cder/ob/docs/patexclnew.cfm?Appl_No=020065&Product_No=001&table1=OB_OTC
Go Links
Patent and Exclusivity Search Results from query on Appl No 020065 Product 001 in the OB_OTC list.
Patent Data
There are no unexpired patents for this product in the Orange Book Database.
[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]
Exclusivity Data
There is no unexpired exclusivity for this product.
View a list of all patent use codes
View a list of all exclusivity codes
Return to Electronic Orange Book Home Page
FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - Monthly
Generic Drug Product Information & Patent Information - Daily
Orange Book Data Updated Through August, 2007
Patent and Generic Drug Product Data Last Updated: September 28, 2007
Done
Local intranet

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/s/

Martin Shimer

10/26/2007 08:17:17 AM

MINOR AMENDMENT

ANDA 78-208

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Medvice Consulting
US Agent for Altaire Pharmaceuticals

TEL: 970-243-5490

FAX: 970-243-5501

ATTN: Martin Dalsing

PROJECT MANAGER: (240) 276-8518

FROM: Rosalyn Adigun

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 15, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Pheniramine.

SPECIAL INSTRUCTIONS:

See Chemistry comments Attached

Please submit your response in electronic format. This will improve document availability to review staff.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (**3** pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78- 208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Drug Master File (DMF) No. (b) (4) has been found deficient. The DMF holder has been informed of the deficiencies. Please do not respond to this letter until you have received notification from the DMF holder that all deficiencies have been addressed, and a DMF amendment has been submitted to the Agency.

2. Drug Master File (DMF) No. (b) (4) has been found deficient. The DMF holder has been informed of the deficiencies. Please do not respond to this letter until you have received notification from the DMF holder that all deficiencies have been addressed, and a DMF amendment has been submitted to the Agency.

3. Please provide (b) (4)

4. The specification for (b) (4) .

5. We note you have provided (b) (4) .

6. Please submit (b) (4) .

7. Please include (b) (4) .

8. Please submit (b) (4) .

9. Please submit [redacted].

10. Please provide [redacted]

11. Please clarify [redacted].

12. Please include [redacted]

13. Please include [redacted].

14. Please include [redacted].

15. Please provide [redacted].

16. We notice that [redacted].

17. Please conduct [redacted]

18. Please revise [redacted].

19. Please include [redacted].

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of approval.

2. Bioequivalence, Microbiology and Labeling information you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under a separate cover.

3. Please conduct your future drug product accelerated stability testing at (40 ºC +/-2 ºC/ 25% RH± 5%RH).

Sincerely yours,

{See appended electronic signature}

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

James Fan
3/3/2008 12:52:07 PM
James M Fan for Rashmikant Patel

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

No 356h form called firm to submit - William Rivers 8/18/08

May 21, 2008

Via Overnight Mail

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attn.: Document Control Room Clerk

RE: Response to Minor Amendment Letter (March 4, 2008) – Chemistry Comments
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution)

To whom it may concern:

Please find enclosed an 'Archival Copy' and 'Chemistry Section' copy of the requested Minor Amendment to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Minor Amendment to ANDA # 78-208 (including attachments) to serve as Altaire's response to the March 4, 2008 request for minor amendment of said submission.

Kindly note that the enclosed Minor Amendment is the fourth (4^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

Please forward the 'Chemistry Section' copy of the Minor Amendment the attention of Ms. Rosalyn Adigun, the assigned Project Manager regarding ANDA 78-208.

We anticipate that said response appropriately addresses the issues raised in the Minor Amendment Letter (of on or about March 4, 2008), and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

Under separate cover, I am forwarding a 'Field Submission' copy of the Minor Amendment to the FDA's District Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel

Encl: as indicated

cc: (w/ encl)

Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION			**REQUEST FOR CONSULTATION**	
TO *(Division/Office)* DHHS/FDA/CDER/OPSS/OSE/DMETS **Request thru: Janet Anderson**			FROM: Beverly Weitzman - beverly.weitzman@fda.hhs.gov HFD-613 - Labeling Review Branch HFD-600 Office of Generic Drugs	
DATE: June 25, 2008	IND NO.	ANDA NO. 78-208	TYPE OF DOCUMENT Proposed Proprietary Name	DATE OF DOCUMENT August 27, 2007
NAME OF DRUG Naphazoline HCl and Pheniramine Maleate		Name & NDA of RLD 20-065 - Opcon-A by Bausch & Lomb	CLASSIFICATION OF DRUG (OTC) OPHTHALMIC SOLUTION	DESIRED COMPLETION DATE 60 to 90 days
NAME OF FIRM Altaire Pharmaceuticals, Inc.				

REASON FOR REQUEST

I. GENERAL

9 NEW PROTOCOL
9 PROGRESS REPORT
9 NEW CORRESPONDENCE
9 DRUG ADVERTISING
9 ADVERSE REACTION REPORT
9 PRE NDA MEETING
9 END OF PHASE II MEETING
9 RESUBMISSION
9 SAFETY/EFFICACY
9 PAPER NDA
9 RESPONSE TO DEFICPENCY LETTER
9 FINAL PRINTED LABELING
9 LABELING REVISION
9 ORIGINAL NEW CORRESPONDENCE
FORMULATIVE REVIEW-+
9 MANUFACTURING CHANGE/ADDITION
9 CONTROL SUPPLEMENT
X *OTHER ('specify below)*
Proposed Proprietary Name: (b) (4)
9 MEETING PLANNED BY

II.BIOMETRICS

STATISTICAL EVALUATION BRANCH	STATISTICAL APPLICATION BRANCH
9 TYPE A OR B NDA REVIEW 9 END QF PHASE II MEETING 9 CONTROLLED STUDI ES 9 PROTOCOL REVIEW 9 OTHER	9 CHEMISTRY 9 PHARMACOLOGY 9 BIOPHARMACEUTICS 9 OTHER

III.BIOPHARMACEUTICS

Γ DISSOLUTION
Γ PROTOCOL-- BIOPHARMACEUTICS
Γ IN--VIVO WAIVER REQUEST
Γ DEFICIENCY LETTER RESPONSE
Γ BIOAVAILABILITY STUDIES
Γ PHASE IV STUDIES

IV.DRUG EXPERIENCE

Γ PHASE IV SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
Γ DRUG USE e.g. POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
Γ CASE REPORTS OF SPECIFIC *REACTIONS(List below)*
Γ COMPARATIVE RISK ASSESSEMENT ON GENERIC DRUG GROUP
Γ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
Γ SUMMARY OF ADVERSE EXPERIENCE
POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

Γ CLINICAL
Γ PRECLINICAL

COMMENTS: Altaire is proposing the use of the trade name (b) (4) Attachments: container and carton labels. The RLD for this product is Opcon - A (NDA 20-065)

SIGNATURE OF REQUESTER **Beverly Weitzman**	METHOD OF DE LIVERY DFS and E-mail
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

FORM FDA 3291 (7/83)

Following this page, 2 pages withheld in full (b)(4)

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

/s/

Beverly Weitzman

6/25/2008 01:27:12 PM

Telephone Fax

ANDA 78-208

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240 276-8984

TO: Medvice Consulting
U.S. Agent for Altaire Pharmaceuticals, Inc.

TEL: 970- 243-5490

FAX: 970-243-5501

ATTN: Martin Dalsing

FROM: Beverly Weitzman

:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for naphazoline hydrochloride and pheniramine maleate ophthalmic solution.

Pages (including cover): 4

SPECIAL INSTRUCTIONS:

Labeling Comments

REVIEW OF PROFESSIONAL LABELING #1
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 78-208

Date of Submission: August 27, 2007

Applicant's Name: Altaire Pharmaceuticals, Inc.

Established Name: Naphazoline hydrochloride 0.027% and Pheniramine maleate 0.315% and ophthalmic solution, USP (OTC)

Labeling Deficiencies:

1. **GENERAL COMMENTS:**

   a. We have forwarded your proposed proprietary name, [redacted] (b) (4) to the Division of Medication Errors and Technical Support (DMETS), for review and comment. We will inform you of their comments when they become available to us.

   b. Please note that your drug product is the subject of a USP monograph. We encourage you to include USP in the established name of your drug product.

2. **CONTAINER** (15 mL and 30 mL)

   a. **PRINCIPLE DISPLAY PANEL**: 21 CFR 201.61 (b) requires a statement of identity, **consisting of the established name of the drug** appearing on the principal display panel of an over-the-counter drug package. In addition, please note in that in accordance with 21 CRF 201.61 (c) the statement of identity shall be presented in bold face type on the principal display panel, and shall be in a size reasonably related to the most prominent printed matters on the principle display panel. Revise to include the established names and concentrations of the active ingredients **"naphazoline hydrochloride 0.027% and pherniramine maleate 0.315% ophthalmic solution, USP"** following your proposed proprietary name.

   b. Revise your storage temperature to read as "store at 20°-25°C (68°-77°F)".

   c. In order for us to verify your compliance with the labeling format requirements of 21 CFR 201.66 (Format and content of OTC labeling), please submit a format legend for each size of your labels.

   d. Bold the pharmacological category **"Itching and Redness Reliever Eye Drops".** Refer to 21 CRF 201.61 (c) for further guidance.

   e. Inactive ingredients: Revise [redacted] (b) (4) to read as "purified water" to be consistent with your "components and composition" statement.

   f. Delete [redacted] (b) (4)

   g. It is difficult to read the information on your container label. Please note that it is not necessary to have all the required information for an OTC product placed on your container label when there is an outside container (carton) provided with all the required information. Refer to 21 CRF 201.66 (c) for further guidance. Please revise you container label to be the same as the reference listed drug, Opcon-A (NDA 20-065/S-017: Approved July 31, 2007). We refer you to http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm

3. **CARTON:** (15 mL and 30 mL)

   a. See **CONTAINER** COMMENTS (a) through (e).

   b. **Side Panel and Back Panel-Top Flap** – Include the established names and concentrations of the active ingredients, **naphazoline hydrochloride 0.027% and pheniramine maleate 0.315% ophthalmic solution, USP** following your proposed proprietary name.

   c. **PRINCIPAL DISPLAY PANEL**: Delete "Available without a prescription" as this information appears on the side panel.

   d. Add the statement "With antihistamine to relieve itching" as does the reference listed drug.

4. **PATIENT INFORMATION SHEET:**

   a. Include the established names and concentrations of the active ingredients, **naphazoline hydrochloride 0.027% and pheniramine maleate 0.315% ophthalmic solution, USP** following your proposed proprietary name.

   b. See Container comment (b) and (e).

Revise your labeling, as instructed above, and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

To facilitate review of your next submission, please provide a side-by-side comparison of your proposed labeling with that of your last submission with all differences annotated and explained.

{See appended electronic signature page}

_____

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

John Grace
8/6/2008 12:01:28 PM
for Wm Peter Rickman

COMPLETE RESPONSE -- MINOR

ANDA 78-208

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Medvice Consulting TEL: 970-243-5490

ATTN: Martin Dalsing FAX: 970-243-5501

FROM: Rosalyn Adigun FDA CONTACT PHONE: (240) 276-8518

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated March 15, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Pheniramine Maleate 0.315% and Naphazoline Hydrochloride 0.027% Ophthalmic Solution.

Reference is also made to your amendment dated May 21, 2008.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format.
This will improve document availability to review staff.

We have completed the review of your ANDA and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues in the following attachments (_2___ pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. Upon OGD's acceptance for filing of your ANDA, it was determined that an adequate amount of information was submitted to allow for review of your Bioequivalence and Microbiology data. You will be notified in a separate communication of any further deficiencies identified during our review of your Bioequivalence and Microbiology data If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78- 208 APPLICANT: Altaire Pharmaceuticals, Inc.

DRUG PRODUCT: Pheniramine Maleate 0.315% and Naphazoline Hydrochloride 0.027% Ophthalmic Solution

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please provide [redacted (b) (4)].
2. Please provide [redacted (b) (4)].
3. Please provide [redacted (b) (4)].
4. Please provide [redacted (b) (4)].
5. Please provide [redacted (b) (4)].
6. The validation of [redacted (b) (4)]
7. Please provide [redacted (b) (4)]
8. Please provide [redacted (b) (4)]
9. Please provide [redacted (b) (4)]

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. The firms referenced in your application should be in compliance with cGMP at the time of approval.

2. Labeling deficiencies were communicated to you via facsimile on August 6, 2008. Please address the labeling deficiencies in the August 6, 2008 communication prior to or concurrent with your response to this communication.

3. Bioequivalence and Microbiology you have provided is pending review. After the reviews are completed, any deficiencies found will be communicated to you under a separate cover.

Sincerely yours,

{See appended electronic signature page}

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

James Fan
8/19/2008 07:59:22 AM
James M Fan for Rashmikant Patel

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

September 9, 2008

Via Overnight Mail

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

N-000-AM

Attn.: Document Control Room Clerk

RE: Response to Minor Amendment Letter - August 19, 2008
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution)

To whom it may concern:

Please find enclosed an 'Archival Copy' and 'Chemistry Section' copy of the requested Minor Amendment to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Minor Amendment to ANDA # 78-208 (including attachments) to serve as Altaire's response to the August 19, 2008 request for minor amendment of said submission.

Kindly note that the enclosed Minor Amendment is the fifth (5^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

Please forward the 'Chemistry Section' copy of the Minor Amendment the attention of Ms. Rosalyn Adigun, the assigned Project Manager regarding ANDA 78-208.

We anticipate that said response appropriately addresses the issues raised in the Minor Amendment Letter (of on or about August 19, 2008), and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

Under separate cover, I am forwarding a 'Field Submission' copy of the Minor Amendment to the FDA's District Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel

Encl: as indicated

cc: (w/ encl)

Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855-2773 (240-276-8408)

TO: Martin Dalsing		**FROM:** Bonnie McNeal
Medvice Consulting		Microbiology Project Manager
PHONE: 970-243-5490		**PHONE:** (240) 276-8831
FAX: 970-243-5501		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: **4**

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for ANDA 78-208 for Naphazoline and Pheniramine. The submissions reviewed were submitted on March 15 and June 26, 2006; and August 27, 2007. Please respond to this communication as quickly as possible. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review. The response to this communication will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT-RESPONSE TO MICROBIOLOGY DEFICIENCIES should appear prominently in your cover letter.

Should you also have other outstanding deficiencies, for review purposes, please attempt to consolidate your responses into a single submission for this application.

If you have questions, feel free to call Bonnie McNeal or Mark Anderson.

LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 78-208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

A. Microbiology Deficiencies:

1. Regarding Composition of the Drug Product:
   a. Please identify (b) (4)

2. (b) (4)

3.

4.

Following this page, 1 page withheld in full (b)(4)

9. (b) (4)

10

11

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

For future submissions and ease of review, please consult the Agency's 1994 "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products".

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Lynne Ensor
9/19/2008 01:17:06 PM

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

CHEM COPY

RECEIVED
OCT 2 1 2008
OGD

Response To Microbiology Deficiencies
(as per Minor Amendment Letter - September 19, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

N/AS

A. RESPONSE TO CITED MICROBIOLOGY DEFICIENCIES

(b) (4)

[redacted]

Following this page, 42 pages withheld in full (b)(4)

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Response To Microbiology Deficiencies
(as per Minor Amendment Letter - September 19, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution

B. NOTES AND ACKNOWLEDGMENTS

1. For future submissions, Altaire will consult and make all reasonable efforts to conform to the Agency's 1994 "Guidance for Industry for the Submission of Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products."

Respectfully Submitted;

Michael S. Sawaya
General Counsel
Altaire Pharmaceuticals, Inc.
October 16, 2008

OFFICIAL CORRESPONDENT:
Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855-2773 (240-276-8408)

TO: Martin Dalsing		**FROM:** Bonnie McNeal
Medvice Consulting		Microbiology Project Manager
PHONE: 970-243-5490		**PHONE:** (240) 276-8831
FAX: 970-243-5501		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: **4**

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for ANDA 78-208 for Naphazoline and Pheniramine. The submission reviewed was submitted on October 16, 2008. Please respond to this communication as quickly as possible. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review. The response to this communication will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT-RESPONSE TO MICROBIOLOGY DEFICIENCIES should appear prominently in your cover letter.

Should you also have other outstanding deficiencies, for review purposes, please attempt to consolidate your responses into a single submission for this application.

If you have questions, feel free to call Bonnie McNeal or Mark Anderson.

LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 78-208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

Microbiology Deficiencies:

1. (b) (4)

2.

3.

Following this page, 1 page withheld in full (b)(4)

7. (b) (4)

Please clearly identify your amendment to this facsimile as “RESPONSE TO MICROBIOLOGY DEFICIENCIES”. The “RESPONSE TO MICROBIOLOGY DEFICIENCIES” should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Lynne Ensor
11/24/2008 07:02:06 AM

BIOEQUIVALENCE AMENDMENT

ANDA 78-208

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Altaire Pharmaceuticals, Inc. TEL: 970-243-5490

ATTN: Martin Dalsing FAX: 970-243-5501

FROM: Diana Solana-Sodeinde FDA CONTACT PHONE: (240)276-8782

Dear Sir:

This facsimile is in reference to the bioequivalence data submitted on August 27, 2007, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Naphazoline Hydrochloride 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution/Drops.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached **two** pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all the deficiencies listed. **Facsimiles or partial replies will not be considered for review**, nor will the review clock be reactivated until all deficiencies have been addressed. Your cover letter should clearly indicate that the response is a "Bioequivalence Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

Please remember that when changes are requested to your proposed dissolution methods and/or specifications by the Division of Bioequivalence, an amendment to the Division of Chemistry should also be submitted to revise the release and stability specification. We also recommend that supportive dissolution data or scientific justification be provided in the CMC submission to demonstrate that the revised dissolution specification will be met over the shelf life of the drug product.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format.
This will improve document availability to review staff.

ANDA:	78-208
APPLICANT:	Altaire Pharmaceuticals, Inc.
DRUG PRODUCT:	Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops

The Division of Bioequivalence (DBE) has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiency has been identified:

Your requested waiver of *in vivo* bioequivalence (BE) study requirements for your test product, Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops does not meet the requirements set forth in Section 21 CFR § 320.22 (b) (1). Your test product formulation is qualitatively (Q1) but not quantitatively (Q2) the same as the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb. Therefore, the waiver request is denied.

The DBE currently recommends the following options:

a. In order to obtain a waiver of *in vivo* bioequivalence testing for your test product under 21 CFR § 320.22(b) (1):

   i) Please reformulate your test product to match qualitatively and quantitatively to the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution);

   ii) In addition, please submit comparative chemico-physical data, which should include but not be limited to pH, specific gravity, osmolality and viscosity, for the newly reformulated test product versus RLD product.

b. Alternatively, if you decide not to reformulate the current test formulation and to have the current test formulation be considered under 21 CFR § 314.94 (a) (9) (iv), please conduct a bioequivalence study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. You may submit a protocol to the Office of Generic Drugs prior to initiation of your study, for review and comments.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Dale Conner

12/16/2008 02:52:34 PM

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

January 13, 2009

Via UPS Ground Delivery

ORIG AMENDMENT
N-000-AS

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attn.: Document Control Room Clerk

RE: Minor Amendment - Response to Microbiology Deficiencies (November 24, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution)

To whom it may concern:

Please find enclosed an 'Archival Copy' and 'Microbiology Section' copy of the requested Minor Amendment to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Minor Amendment to ANDA # 78-208 (including attachments) to serve as Altaire's response to the November 24, 2008 request for a minor amendment – microbiology deficiencies of said submission.

Kindly note that the enclosed Minor Amendment is the ninth (9^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

Please forward the 'Microbiology Section' copy of the Minor Amendment the attention of Ms. Bonnie McNeal, the assigned Microbiology Project Manager regarding ANDA 78-208.

We anticipate that this response appropriately addresses the issues raised in the November 24, 2008 Minor Amendment Letter regarding microbiology deficiencies, and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

RECEIVED
JAN 15 2009
OGD

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Under separate cover, I am forwarding a 'Field Submission' copy of the Minor Amendment to the FDA's District Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel

Encl: as indicated

cc: (w/o encl)
Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Bioequivalence Amendment
(as per Deficiency Letter – December 17, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Naphazoline HCl 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution

RESPONSE TO CITED BIOEQUIVAELNCE DEFICIENCIES

Altaire has re-formulated the Proposed Drug Product 'Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution' to qualitatively and quantitatively[1] match the Reference Drug Product Opcon-A ® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution). Attached hereto at 'Appendix A' is a copy of the proposed re-formulation, and what follows is a review of the re-formulation process and results.

I. SIDE BY SIDE FORMULATION COMPARISON

Components and composition of the re-formulated Proposed Drug Product and the Reference Drug Product are reflected on the tables below. Review of the data presented therein demonstrates that:

(i) the concentrations or amounts of all ingredients (inactive ingredient(s), APIs and the preservative) in the proposed re-formulation of the Proposed Drug Product are within ± 5 percent of the concentrations or amounts of the Reference Drug Product; and

(ii) the re-formulated Proposed Drug Product and the Reference Drug Product present equivalent chemico-physical data.

Based upon such data, it is Altaire's position that the re-formulated Proposed Drug Product meets the criteria for a bioequivalency waiver pursuant to 21 CFR 320.22 (b) (1). Accordingly, we respectfully request that the Proposed Drug Product be granted a waiver of *in vivo* bioequivalence study requirements.

[1] Pursuant to the undersigned's January 14, 2009, teleconference with the reviewer assigned by the Division of Bioequivalence, quantitative bioequivalence of a proposed drug product to a reference drug product requires that the "concentration or amount of the inactive ingredient(s) in the test product . . .not differ by more than a ± 5 percent of the concentration or amount in the reference listed drug." *See* 'Guidance for Industry – Bioavailability and Bioequivalence Study for Nasal Aerosols and Nasal Sprays for Local Action', CDER, Biopharmaceutics, April 2003.

Following this page, 6 pages withheld in full (b)(4)

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Bioequivalence Amendment
(as per Deficiency Letter – December 17, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Naphazoline HCl 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution

(b) (4)

[redacted]

III. COMMITMENT FOR FURTHER VALIDATION AND STABILIYY EXERCISES

Upon granting of the requested bioequivalency waiver for the proposed re-formulation, Altaire commits to issuing three (3) batches of the re-formulated Proposed Drug Product for a process control validation exercise. Samples randomly collected from the process validation batches will be subjected to Accelerated (through three [3] months) and Controlled Room Temperature (through twenty-four [24] months) stability exercises. All results shall be reviewed and summarized, and submitted for further review in support of ANDA 78-208.

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

Bioequivalence Amendment
(as per Deficiency Letter – December 17, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Naphazoline HCl 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution

IV. CONCLUSION

Altaire anticipates that the above response appropriately addresses the concerns indicated in the Bioequivalence Deficiency Letter of December 17, 2008. Specifically, we believe that the data enclosed herein demonstrates that the re-formulated Proposed Drug Product meets the criteria for a bioequivalency waiver pursuant to 21 CFR 320.22 (b) (1). Accordingly, we respectfully request that the re-formulation of the Proposed Drug Product be granted a waiver of *in vivo* bioequivalence study requirements.

Respectfully Submitted;

Michael S. Sawaya
General Counsel
Altaire Pharmaceuticals, Inc.
February 2, 2009

OFFICIAL CORRESPONDENT:
Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Ave.
Grand Junction, CO 81501
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 ◦ 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 ◦ Fax: 631.722.9683

February 3, 2009

Via UPS Ground Delivery

N-000-AB

Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

RE: Bioequivalence Amendment - Response to Bioequivalence Deficiencies (December 17, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution)

To whom it may concern:

Please find enclosed a 'Field Submission' copy of the requested Bioequivalence Amendment to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Bioequivalence Amendment to ANDA # 78-208 (including attachments) to serve as Altaire's response to the December 17, 2008, request for a Bioequivalence Amendment - Response to Bioequivalence Deficiencies of said submission.

Kindly note that the enclosed Minor Amendment is the tenth (10^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

We anticipate that this response appropriately addresses the issues raised in the December 17, 2008, request for a Bioequivalence Amendment - Response to Bioequivalence Deficiencies, and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

Under separate cover, I am forwarding an 'Archival Copy' and 'Pharmacokinetic Copy" of the Bioequivalence Amendment to the attention of the Document Control Room Clerk, Office of Generic Drugs, CDER, FDA in Rockville, MD.

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel

Encl: as indicated

cc: (w/o encl)

Attn.: Document Control Room Clerk
Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505

BIOEQUIVALENCE AMENDMENT

ANDA 78-208

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Altaire Pharmaceuticals, Inc. TEL: 970-243-5490

ATTN: Martin Dalsing FAX: 970-243-5501

FROM: Diana Solana-Sodeinde FDA CONTACT PHONE: (240) 276-8782

Dear Sir:

This facsimile is in reference to the bioequivalence data submitted on August 27, 2007, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Naphazoline Hydrochloride 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution/Drops.

Reference is also made to your amendments dated February 2, 2009 and February 3, 2009.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached **two** pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all the deficiencies listed. **Facsimiles or partial replies will not be considered for review**, nor will the review clock be reactivated until all deficiencies have been addressed. Your cover letter should clearly indicate that the response is a "Bioequivalence Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

Please remember that when changes are requested to your proposed dissolution methods and/or specifications by the Division of Bioequivalence, an amendment to the Division of Chemistry should also be submitted to revise the release and stability specification. We also recommend that supportive dissolution data or scientific justification be provided in the CMC submission to demonstrate that the revised dissolution specification will be met over the shelf life of the drug product.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format.
This will improve document availability to review staff.

ANDA:	78-208
APPLICANT:	Altaire Pharmaceuticals, Inc.
DRUG PRODUCT:	Naphazoline HCL & Pheniramine Maleate (0.027% & 0.315%) Ophthalmic Solution/Drops

The Division of Bioequivalence (DBE) has completed its review of your submission(s) acknowledged on the cover sheet. The following deficiency has been identified:

Your **reformulated** Naphazoline HCl 0.027% & Pheniramine Maleate 0.315% Ophthalmic Solution/Drops is now qualitatively (Q1) but not quantitatively (Q2) the same as the formulation of the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution), manufactured by Bausch and Lomb. The amount of (b) (4) in your reformulated product is not the same as that in the RLD product. Therefore, the waiver request is still denied at this time.

As stated in our previous deficiency letter to you, the DBE currently recommends the following options:

1. In order to obtain a waiver of *in vivo* bioequivalence testing for your test product under 21 CFR § 320.22(b)(1):

   a) Please reformulate the quantity of (b) (4) in your test product to be quantitatively the same as in the reference listed drug (RLD) product, Opcon-A® (Naphazoline HCl 0.02675% & Pheniramine Maleate 0.315% Ophthalmic Solution); and in addition,

   b) Please submit comparative chemico-physical data, which should include but not be limited to pH, specific gravity, osmolality and viscosity, for the newly reformulated test product versus RLD product. The comparative data on specific gravity, pH, osmolality, tonicity and viscosity for the test and RLD products should be provided using the Exhibit (reformulated) test lot, and two (2) other production lots, if available, of the test product, and three (3) commercial lots of the RLD product. The measurement should be done in triplicate for each lot tested.

It is advisable that you submit the reformulated composition for review prior to conducting additional testing to characterize the chemico-physical properties of the reformulated product in comparison with the RLD product.

2. Alternatively, if you decide not to reformulate the current test formulation and to have the current test formulation be considered under 21 CFR § 314.94 (a) (9) (iv), please conduct a bioequivalence study with a clinical endpoint to demonstrate equivalent safety and efficacy between the test and RLD products. You may submit a protocol to the Office of Generic Drugs prior to initiation of your study, for review and comments.

Sincerely yours,

{See appended electronic signature page}

Dale P. Conner, Pharm.D.
Director, Division of Bioequivalence I
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Dale Conner

2/17/2009 01:36:28 PM

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

February 20, 2009

Via UPS Ground Delivery

ORIG AMENDMENT
N-000-AF

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RECEIVED
FEB 23 2009
OGD

Attn.: Document Control Room Clerk

RE: Labeling Amendment - Response to Labeling Review (December 17, 2008)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Proposed Drug Product – Naphazoline HCl 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution)

To whom it may concern:

Please find enclosed an 'Archival Copy' and a 'Labeling Review' copy of the Labeling Amendment to Altaire's pending ANDA # 78-208 (Drug Product – Naphazoline HCl 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution). Kindly allow the enclosed copies of the Labeling Amendment to ANDA # 78-208 (including attachments) to serve as Altaire's response to the December 17, 2008, Labeling Review.

Please forward the 'Labeling Review' (red jacket) copy of the Labeling Amendment to the attention of the assigned reviewer, Ms. Beverly Weitzman, Division of Labeling and Program Support, Labeling Review Branch.

Kindly note that the enclosed Labeling Amendment is the eleventh (11^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

We anticipate that this Labeling Amendment appropriately addresses the issues raised in the December 17, 2008, Labeling Review, and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

Under separate cover, I am forwarding a 'Field Submission' copy of the Labeling Amendment to the FDA's District Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel

Encl: as indicated

cc: (w/o encl)
Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

March 3, 2009

ORIG AMENDMENT

N.A.B

RECEIVED

MAR 04 2009

OGD

Via UPS Ground Delivery

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attn.: Document Control Room Clerk

RE: Bioequivalence Amendment II - Response to Bioequivalence Deficiencies (February 17, 2009)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution)

To whom it may concern:

Please find enclosed an 'Archival Copy' and 'Pharmacokinetic Section' copy of the requested Bioequivalence Amendment II to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Bioequivalence Amendment II to ANDA # 78-208 (including attachments) to serve as Altaire's response to the February 17, 2009 request for a Bioequivalence Amendment.

Kindly note that the enclosed Bioequivalence Amendment II is the eleventh (11^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

Please forward the 'Review' (Pharmacokinetic Section - orange jacket) copy of Bioequivalence Amendment II to the attention of Ms. Diana Solana-Sodeinde, Division of Bioequivalence I.

We anticipate that this response appropriately addresses the issues raised in the February 17, 2009 request for a Bioequivalence Amendment, and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

We have also copied the FDA's District Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433, with a 'Field Submission' copy of Bioequivalence Amendment II.

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted:

Michael S. Sawaya
General Counsel

Encl: as indicated

cc:
(w/ encl)
Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

(w/o encl)
Mr. Martin Dalsing
Medvice Consulting Inc.
Grand Valley Business Plaza
2214 Sanford Drive, Suite B7
Grand Junction, Colorado 82505

FAX – Microbiology Deficiencies Enclosed

Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville MD 20855-2773 (240-276-8408)

TO: Martin Dalsing		**FROM:** Bonnie McNeal
Medvice Consulting		Microbiology Project Manager
PHONE: 970-243-5490		**PHONE:** (240) 276-8831
FAX: 970-243-5501		**FAX:** (240) 276-8725

Total number of pages, excluding this cover sheet: **3**

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

Microbiology Deficiencies:

Enclosed are the microbiology deficiencies for ANDA 78-208 for Naphazoline and Pheniramine. The submission reviewed was submitted on January 13, 2009. Please respond to this communication as quickly as possible. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review. The response to this communication will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT-RESPONSE TO MICROBIOLOGY DEFICIENCIES should appear prominently in your cover letter.

Should you also have other outstanding deficiencies, for review purposes, please attempt to consolidate your responses into a single submission for this application.

If you have questions, feel free to call Bonnie McNeal or Mark Anderson.

LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS

ANDA: 78-208 APPLICANT: Altaire Pharmaceuticals

DRUG PRODUCT: Pheniramine Maleate 0.315% & Naphazoline HCl 0.027%

Microbiology Deficiencies:

1. (b) (4)

2.

(b) (4)

Please clearly identify your amendment to this facsimile as "RESPONSE TO MICROBIOLOGY DEFICIENCIES". The "RESPONSE TO MICROBIOLOGY DEFICIENCIES" should also be noted in your cover page/letter.

Sincerely yours,

{See appended electronic signature page}

Lynne A. Ensor, Ph.D.
Microbiology Team Leader
Office of Generic Drugs
Center for Drug Evaluation and Research

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

/s/

Lynne Ensor
3/4/2009 07:39:39 AM

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

March 18, 2009

Via UPS Ground Delivery

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

ORIG AMENDMENT

RECEIVED
MAR 20 2009
OGD

Attn.: Document Control Room Clerk

RE: Microbiology Amendment III - Response to Microbiology Deficiencies (March 4, 2009)
ANDA # 78-208
Applicant: Altaire Pharmaceuticals, Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution)

To whom it may concern:

Please find enclosed an 'Archival Copy' and 'Microbiology Section' copy of the requested Microbiology Amendment III to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCl 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Microbiology Amendment III to ANDA # 78-208 (including attachments) to serve as Altaire's response to the March 4, 2009 request for a Microbiology Amendment.

Kindly note that the enclosed Microbiology Amendment III is the twelfth (12^{th}) volume submitted as of the date of this letter in support of ANDA 78-208.

Please forward the 'Review' (Microbiology Section - orange jacket) copy of Microbiology Amendment III to the attention of Ms. Bonnie McNeal, Microbiology Project Manager.

We anticipate that this response appropriately addresses the issues raised in the March 4, 2009 request for a Microbiology Amendment, and respectfully request that such be construed as an amendment to the original submission of ANDA 78-208.

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

We have also copied the FDA's District Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433, with a 'Field Submission' copy of Microbiology Amendment III.

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501
Tel: (970) 243-5490 Fax: (970) 243-5501
E-mail: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel

Encl: as indicated

cc:
(w/ encl)
Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

(w/o encl)
Mr. Martin Dalsing
Medvice Consulting Inc.
806 Kimball Avenue
Grand Junction, Colorado 81501

From: West, Robert L
Sent: Friday, February 05, 2010 8:56 AM
To: Tran, Trang
Subject: RE: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

Trang:

Please place the email in DARRTS for 78-208. When the first-generic audit is completed, we can turn the AP into an N/A (minor) based upon cGMPs.

Thanks,

Bob

From: Tran, Trang
Sent: Friday, February 05, 2010 8:52 AM
To: West, Robert L
Subject: FW: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

FYI

From: CDER EESQUESTIONS
Sent: Friday, February 05, 2010 8:52 AM
To: Tran, Trang
Subject: RE: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

Dear Trang,

The INT-DO indicates that (b) (4) .

Kind Regards,

April

APRIL INYARD, PHD.
Staff Fellow
CDER/OC/DMPQ/MAPCB
april.inyard@fda.hhs.gov

From: Inyard, April
Sent: Friday, February 05, 2010 7:56 AM
To: CDER EESQUESTIONS
Subject: FW: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

From: Tran, Trang
Sent: Friday, February 05, 2010 7:19 AM
To: Inyard, April
Subject: RE: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

Good morning April,

Could you please let me know when the inspections for this ANDA will be scheduled? This application is very close to approval and it's the first generic. It would be greatly appreciated if you can expedite the process.

Thanks,

Trang

From: Inyard, April
Sent: Thursday, January 07, 2010 10:26 AM
To: Tran, Trang
Subject: RE: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

Dear Trang,

The inspection request is still pending assignment.

Kind Regards,

April

APRIL INYARD, PHD.
Staff Fellow
CDER/OC/DMPQ/MAPCB
april.inyard@fda.hhs.gov

From: Tran, Trang
Sent: Wednesday, January 06, 2010 4:29 PM
To: CDER EESQUESTIONS
Subject: ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

Hi,

I'd like to request for the EES status of the above ANDA. The last assigned inspection for (b) (4) **was on** (b) (4)
Thanks,

Trang

Trang Q. Tran, Pharm.D.
Chemistry PM, Team 3
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research, FDA
Phone: (240) 276-8518
Fax: (240) 276-8504

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
ANDA-78208	ORIG-1	ALTAIRE PHARMACEUTICALS INC	NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE

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

/s/

TRANG Q TRAN
02/05/2010

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

March 15, 2010

SD#16

Via UPS Ground Delivery

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attn: Document Control Room Clerk

RE: Telephone Amendment- Response to Chemistry Review Request of February 26th, 2010
ANDA # 78-208
Applicant: Altaire Pharmaceuticals Inc.
Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCL 0.027% Ophthalmic Solution

To Whom It May Concern:

Please find enclosed an 'Archival Copy' and a 'Chemistry Section' copy of the requested Telephone Amendment to Altaire's pending ANDA # 78-208 (Drug Product – Pheniramine Maleate 0.315% and Naphazoline HCL 0.027% Ophthalmic Solution). Kindly allow the enclosed copies of the Telephone Amendment to ANDA # 78-208 (including attachments) to serve as Altaire's response to the February 26th 2010 Request of the Chemistry Review Team.

Kindly note that the enclosed Telephone Amendment is the thirteenth (13th) volume submitted as of the date of this letter in support of ANDA 78-208.

Please forward the Chemistry Section (red jacket) copy of the Telephone Amendment to the attention of Ms. Trang Q. Tran, Chemistry Review Team Leader.

We anticipate that this response appropriately addresses the issues raised on February 26th, 2010 by the Chemistry Review Team, and respectfully request that such be construed as an amendment to the original submission of ANDA # 78-208.

ALTAIRE Pharmaceuticals, Inc.
P.O. Box 849 • 311 West Lane
Aquebogue, N.Y. 11931
Telephone: 631.722.5988 • Fax: 631.722.9683

We have also copied the FDA's Distract Office with jurisdiction over Altaire, specifically the office located at 158-15 Liberty Avenue, Jamaica, NY 11433, with a 'Field Submission' copy of Telephone Amendment.

Should additional information be required, kindly contact the official correspondent for this submission (and Altaire's US Consultant) as follows:

Martin Dalsing
Medvice Consulting Inc.
Kimball Ave.
Grand Junction, CO 81501
Tel : (970) 243-5490 Fax: (970) 243-5501
Email: marty@FDApproval.com

Respectfully Submitted;

Michael S. Sawaya
General Counsel
Altaire Pharmaceuticals, Inc

Encl: as indicated

Cc:
(w/encl)
Food and Drug Administration
District Office
158-15 Liberty Avenue
Jamaica, NY 11433

(w/o encl)
Martin Dalsing
Medvice Consulting Inc.
Kimball Ave.
Grand Junction, CO 8150

OGD APPROVAL ROUTING SUMMARY

ANDA # 78-208 ApplicantAltaire Pharmaceuticals, Inc.
Drug Naphazoline Hydrochloride 0.027% and Pheniramine Maleate 0.315% Ophthalmic Solution Strength(s)_____

APPROVAL ☒ **TENTATIVE APPROVAL** ☐ **SUPPLEMENTAL APPROVAL (NEW STRENGTH)** ☐ **OTHER** ☐

REVIEWER:	**DRAFT Package**	**FINAL Package**
1. **Martin Shimer** Chief, Reg. Support Branch	Date11 Jan 2010 InitialsMHS	Date 9/26/10 Initials rlw/for

Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92) Pediatric Exclusivity System
RLD =Opcon-A NDA#20-065
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked N/A
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐ Written request issued ☐
Was applicant sued w/in 45 days:Yes ☐ No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐ Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒
Date of latest Labeling Review/Approval Summary _____
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒
Type of Letter:Full Approval.
Comments:ANDA submitted on 3/16/2006, BOS=Opcon A NDA 20-065, PII no exclusivity. RTR issued on 5/11/2006. Firm responded to RTR and ANDA was ACK for filing on 8/28/2007. There are no remaining unexpired patents or exclusivities which protect the RLD. This ANDA is eligible for immediate Full Approval.

2. Project Manager, Nitin Patel Team 3 Review Support Branch Date10/13/2009 Date9/27/10
InitialsNP Initials TT

Original Rec'd date3/15/2006 EER Status Pending ☐ Acceptable ☒ OAI ☐
Date Acceptable for Filing3/16/2006 Date of EER Status 9/2/10
Patent Certification (type)II Date of Office Bio Review 3/16/2009
Date Patent/Exclus.expires N/A Date of Labeling Approv. Sum 3/17/2009
Citizens' Petition/Legal Case Yes☐ No ☒ Labeling Acceptable Email Rec'd Yes ☒ No ☐
(If YES, attach email from PM to CP coord) Labeling Acceptable Email filed Yes ☒ No ☐
First Generic Yes ☒ No ☐ Date of Sterility Assur. App. 5/1/2009
Priority Approval Yes ☐ No ☒ Methods Val. Samples Pending Yes ☐ No ☒
(If yes, prepare Draft Press Release, Email it to Cecelia Parise) MV Commitment Rcd. from Firm Yes ☐ No ☐
Acceptable Bio reviews tabbed Yes ☐ No ☒ Modified-release dosage form: Yes ☐ No ☒
Bio Review Filed Electronically:Yes ☒ No ☐ Interim Dissol. Specs in AP Ltr: Yes ☐
Suitability Petition/Pediatric Waiver Yes ☐
Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐
Previously reviewed and tentatively approved ☐ Date _____
Previously reviewed and CGMP def. /NA Minor issued ☐ Date _____
Comments:

3. Labeling Endorsement

Reviewer: Labeling Team Leader:

Date9/21/10 Date9/21/10

Name/InitialsBW Name/InitialsJG

Comments:

From: Grace, John F
Sent: Tuesday, September 21, 2010 9:45 AM
To: Weitzman, Beverly
Cc: Tran, Trang
Subject: RE: Request for labeling endorsement for ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

concur.

From: Weitzman, Beverly
Sent: Tuesday, September 21, 2010 6:26 AM
To: Grace, John F
Cc: Tran, Trang
Subject: RE: Request for labeling endorsement for ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

The labeling review done by Beverly Weitzman 3/17/09 and signed off by John Grace 3/17/09 remains acceptable. There are no new changes to the RLD labeling at this time. No changes noted

---

From: Tran, Trang
Sent: Monday, September 20, 2010 4:08 PM
To: Weitzman, Beverly; Grace, John F
Subject: Request for labeling endorsement for ANDA-078208 Product Name: NAPHAZOLINE HYDROCHLORIDE;PHENIRAMINE MALEATE Dosage Form: SOLUTION, DROPS Applicant: ALTAIRE PHARMACEUTICALS INC

Hi Beverly/John,

Could you please send me the labeling endorsement for the above ANDA? Attached are the copies of the Labeling Approval Summary and the AP letter.

Thanks,

Trang

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date 9/26/10

OGD Regulatory Counsel, Post-MMA Language Included ☐ Initials rlw/for

Comments:N/A. There are no patents currently listed in the "Orange Book" for this drug product.

5. Div. Dir./Deputy Dir. Date9/20/10
Chemistry Div. I Initials PS

Comments:CMC ok,

6. Frank Holcombe **First Generics Only** Date4/2/10
Assoc. Dir. For Chemistry Initialsrmp Comments: (First generic drug review)
CMC is satisfactory for the FGAA.

7. Vacant Date_____ Deputy Dir., DLPS
Initials_____
RLD = Opcon-A Ophthalmic Solution 0.027%/0.315%
Bausch & Lomb, Inc. NDA 20-065

8. Peter Rickman Date9/26/10
Director, DLPS Initials rlw/for
Para.IV Patent Cert: Yes☐ No☐;Pending Legal Action: Yes ☐ No ☐; Petition: Yes☐ No☐ Comments: Bioequivalence waiver granted under 21 CFR 320.22(b)(1). Drug product is "Q&Q" to the RLD. Office-level bio endorsed 3/16/09.

Microbiology/Sterility Assurance found acceptable for approval (Microbiology Review #4) 5/1/09.

Final-printed labeling (FPL) found acceptable for approval 3/17/09, as endorsed 9/21/10.

CMC found acceptable for approval (Chemistry Review #4).

OR

8. Robert L. West Date 9/26/10
Deputy Director, OGD Initials RLWest
Para.IV Patent Cert: Yes☐ No☒; Pending Legal Action: Yes☐ No☒; Petition: Yes☐ No☒
Press Release Acceptable ☐
Comments: Acceptable EEs dated 9/2/10 (Verified 9/26/10). No "OAI" Alerts noted.

There are no patents or exclusivity listed in the current "Orange Book" for this over-the-counter (OTC) drug product.

This ANDA is recommended for approval.

9. Gary Buehler Date 9/26/10
Director, OGD Initials rlw/for
Comments:for Keith Webber, Ph.D.
First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, Nitin Patel Team 3 Date9/27/10

Review Support Branch Initials _____
_____Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
9/27/10Date notified of approval by phone
9/27/10Date approval letter faxed

FDA Notification:
9/27/10Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
_____Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

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ORANGE BOOK PRINT OFF:

Orange Book: Approved Drug Products with Therapeutic Equivalence Evaluations

Patent and Exclusivity Search Results from query on Appl No 020065 Product 001 in the OB_OTC list.

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There are no unexpired patents for this product in the Orange Book Database.

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There is no unexpired exclusivity for this product.

View a list of all patent use codes
View a list of all exclusivity codes

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FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through August, 2010
Patent and Generic Drug Product Data Last Updated: September 24, 2010

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/s/

TRANG Q TRAN
09/27/2010