Pharmaceutical Division | 8500 Hidden River Parkway Tampa FL 33637 | 813 975 7700 Fax 813 975 7770

June 17, 1998

BIOAVAILABILITY

INITIAL AREA N/A

This is not complete response to 1/27/98 Memo N/A because there has been no amendment to DMF. See Tcon. To be classified as NC /S/ 6/23/98

BAUSCH & LOMB
Healthcare and Optics Worldwide

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

MINOR AMENDMENT

RECEIVED
JUN 18 1998
GENERIC DRUGS

Re: ANDA 74-830
Desmopressin Acetate Nasal Solution, 0.01%
Bioequivalence and Chemistry Amendment

Dear Sir or Madam:

The purpose of this correspondence is to address the Agency's facsimile communications, dated January 21, 1998 and February 23, 1998, for the above referenced application. The information contained in the January 21, 1998 communication was discussed during a January 13, 1998 teleconference between the Agency and Bausch & Lomb Pharmaceuticals, Inc. Enclosed in Attachment A (in Volume 2) of this submission are copies of the January 21, 1998 and February 23, 1998 OGD communications, and a copy of Bausch & Lomb's minutes of the January 13, 1998 teleconference. A copy of the Bausch & Lomb communications of January 30, 1998 and March 10, 1998 are included.

In addition, we reference our January 26, 1998 amendment to the application for a minor revision in the spray device. The review of this amendment is crucial to the completion of the demonstration of equivalence to the reference listed drug.

Page(s) 16

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

Pg. 2-17, 6/17/98

We believe that this correspondence provides a thorough response to the questions raised in the Agency's January 21, 1998 communication. As such, we hope that a rapid review and subsequent product approval will be forthcoming. If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7775 or 813-975-7786 or by fax at 813-975-7757.

Sincerely,

Joseph B. Hawkins

Joseph B. Hawkins
Manager
Regulatory Affairs

Enclosure

Desk Copy of Cover Letter: Gordon Johnston, OGD
Dr. Dale Conner, Division of Bioequivalence
Rita Hassell

BIOEQUIVALENCY DEFICIENCIES TO BE PROVIDED TO THE APPLICANT

ANDA:74830 APPLICANT:Bousch and Lomb

DRUG PRODUCT: Desmopressin acetate nasal spray, 0.01%.

The Division of Bioequivalence has completed its review of your June 17, 1998, amendment. The following deficiencies have been identified:

Page(s) _____

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

The above deficiencies were also conveyed to you during a tele-conference on September 8, 1998.

Sincerely yours,

/S/

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

CC:

ile

X:\NEW\FIRMSAM\BAUSCH\LTRS&REV\74830WI.698
Printed in final on 9/8/98

Endorsements: (Final with Dates)
HFD-658/ SINGH
HFD-655/ NERURKAR
HFD-650/ D. Conne

Deficiency: **Submission date: 6/17/98**

1. **STUDY AMENDMENT** (STA)

Strengths: 0.01%
Outcome: **IC**

CC:

ile

X:\NEW\FIRMSAM\BAUSCH\LTRS&REV\74830WI.698
Printed in final on 9/8/98

Endorsements: (tes)
HFD-658/ SINGH
HFD-655/ NERURKAR
HFD-650/ D. Conner

JAN 9/17/98

Deficiency: **Submission date: 6/17/98**

1. **STUDY AMENDMENT** (STA)

Strengths: 0.01%
Outcome: **IC**

Page(s) 9

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

Mechanical Delivery System
data

Desmopressin Acetate
Nasal Solution (Metered Manual Pump), 0.01%
Reviewer: Gur J.P. Singh
ANDA #74-830
74830WI.698

Bausch & Lomb
8500 Hidden River Ave
Tampa, FL 33637
Submission Date:
June 17, 1998

Review of an ANDA Amendment

On February 8, 1996, Bausch and Lomb submitted an application for the waiver of *in vivo* bioequivalence study requirements for its desmopressin acetate 0.01% nasal solution. The sponsor submitted data to support comparative formulation *and in vitro* performance of its product and the reference product DDAVP® 0.01% solution manufactured by Rhone-Poulenc Rorer. A review of those data was completed on May 13, 1996.

On October 20, 1997, the Office of Generic Drugs requested additional data for some of the *in vitro* performance tests. The sponsor submitted the requested data on November 4, 1997. Based on the review of those data, the Agency requested the sponsor (letter date: January 21, 1998) to repeat the *in vitro* performance tests, including Unit Dose and Uniformity of Unit Dose, Droplet Size Distribution, Spray Pattern, Plume Geometry, and Primming and Tail Off characteristics.

The June 17, 1998, ANDA amendment contains results of tests recommended by the Agency on January 21, 1998. This review is based on data submitted in that amendment.

The *in vitro* performance testing employed the following batches of the test and reference products:

Reference Product:	DDAVP® Lot #XD-4021(Expiry Date: 4/98)[1]
Test Product:	B & L lot #025901 (Manufacture Date: 2/23/98)

For all *in vitro* tests (with the exception of priming) test and reference products were primed by wasting first five actuations.

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[1] All testing on the reference product was performed before April 30, 1998. The innovator has revised the formulation of the reference product. Therefore, the refrigerated reference product (formulation tested in this study) is no longer marketed.

Page(s) 7

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Pg. 2-P

RECOMMENDATION

Data submitted by Bausch and Lomb comparing the *in vitro* performance of its desmopressin acetate (0.01%) nasal spray device with that of the reference listed drug, DDAVP® nasal spray manufactured by Rhone-Poulenc Rorer are incomplete due to comments #3-7. The waiver of *in vivo* bioequivalence study requirements for the test product should be deferred till the sponsor has submitted satisfactory *in vitro* performance data.

Gur J.P. Singh, Ph.D.
Division of Bioequivalence
Review Branch II.

/S/

RD INITIALED SNERURKAR
FT INITIALED SNERURKAR Date: 9/17/1998

CONCUR: Date: 9/21/98

Dale Conner, Pharm. D.
Director
Division of Bioequivalence

GJP Singh 9/4/98 74830WI.698

[illegible]

SEP 22 1998

BIOEQUIVALENCY DEFICIENCIES TO BE PROVIDED TO THE APPLICANT

ANDA:74830 APPLICANT:Bousch and Lomb

DRUG PRODUCT: Desmopressin acetate nasal spray, 0.01%.

The Division of Bioequivalence has completed its review of your June 17, 1998, amendment. The following deficiencies have been identified:

Page(s) 1

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

Pg. 12. 9/22/98

The above deficiencies were also conveyed to you during a tele-conference on September 8, 1998.

Sincerely yours,

/S/

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

Pharmaceutical Division 8500 Hidden River Parkway Tampa FL 33637
813 975 7700 Fax 813 975 7770

BIOAVAILABILITY

FPL

October 6, 1998

ORIG AMENDMENT
N/A

BAUSCH & LOMB
Healthcare and Optics Worldwide

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

Re: ANDA 74-830
Desmopressin Acetate Nasal Solution, 0.01%
Bioequivalence Amendment - and - Labeling Amendment

Dear Sir or Madam:

The purpose of this correspondence is to address the Agency's facsimile communications, dated September 22, 1998. The information contained in the September 22, 1998 communication was discussed during a September 8, 1998 teleconference between the Agency and Bausch & Lomb Pharmaceuticals, Inc.

In response to the deficiencies listed in the communication, the following information is provided:

1. **Reference is made to your statement:**

Page(s) 2

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

RJ. 2-3, 10/6/98

We believe that this correspondence provides a thorough response to the questions raised in the Agency's September 22, 1998 communication. As such, we hope that a rapid review and subsequent product approval will be forthcoming. If you have any questions regarding this correspondence, please contact me at the above address or by telephone at (813) 975-7775 or 813-975-7786 or by fax at 813-975-7757.

Sincerely,

Donald H. Chmielewski

Donald H. Chmielewski
Director
Regulatory Affairs

Enclosure

Desk Copy of Cover Letter: Gordon Johnston, OGD
Dr. Dale Conner, Division of Bioequivalence
Rita Hassall