

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

75-260

APPLICATION NUMBER:

CORRESPONDENCE



Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, Illinois 60053
Phone (847) 967-5600
Fax (847) 967-2211

January 7, 1999

Via Facsimile

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

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FA

**ANDA # 75-260
Tretinoin Topical Solution, USP (Product Code 8151)**

**Re: Telephone Amendment in Response to Telephone Call, Joseph
Buccine to Kamel Egbaria on January 7, 1999**

Dear Dr. Kang:

Per my phone conversation with Joseph Buccine, Morton Grove Pharmaceuticals, Inc., is amending the expiration dating period of 24 months for the package size listed in the application to 19 months.

This telephone amendment is being sent to the Chicago District Office, FDA.

If you need further information, please contact me at 847-967-5600.

Sincerely,

Kamel F. Egbaria
Vice President, Research and Development

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Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, Illinois 60053
Phone (847) 967-5600
Fax (847) 967-2211

January 5, 1999

Via Facsimile

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

NDA ORIG AMENDMENT

N/FA

**ANDA # 75-260
Tretinoin Topical Solution, USP (Product Code 8151)**

**Re: Facsimile Amendment in Response to Telephone Call,
Paul Schwartz to Mary Murphy on December 21,
1998**

Dear Mr. Schwartz:

Per your phone conversation with Mary Murphy on December 21, 1998 concerning MGP's testing for residual solvents in Tretinoin, USP, and your request for 18 month stability testing results, the following information is being provided.

MGP Quality Control Test Record (Form 232) has been revised based on the method used to analyze impurities from solvents which was provided to MGP by _____ in Section VI.B. 1.3, page 21 of 61, of the version of their analytical methods dated June 1997 and received by MGP on November 24, 1998. A copy of this method with the specification follows. The revised blank Quality Control Test Record (MGP Form 232) as well as the form with

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Paul Schwartz, PhD
January 5, 1999
Page Two

test results for Lot # R70173, to include testing for [redacted] performed on 12/30/98 are included here for your review.

As you requested, attached is current controlled room-temperature stability data for the exhibition batch, Lot # A0192.

This facsimile amendment is being sent to the Chicago District Office, FDA.

If you need further information, please contact me at 847-967-5600.

Sincerely,



Kamel F. Egbaria
Vice President, Research and Development

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November 30, 1998

Via Federal Express

Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, Illinois 60053
Phone (847) 967-5600
Fax (847) 967-2211

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

NEW COPY

ANDA # 75-260
Tretinoin Topical Solution, USP (Product Code 8151)

Re: Facsimile Amendment in Response to Deficiency
Letter, Patel to Bordoni, dated November 23, 1998

Dear Mr. Sporn:

Pursuant to 21 CFR 314.120 and to Rashmikant Patel's November 23, 1998, letter (copy enclosed), Morton Grove Pharmaceuticals, Inc., (MGP) is amending the above application. A complete copy of this facsimile amendment is being sent to the Chicago District Office, FDA; and to Rashmikant M. Patel, Ph.D., Director, Division of Chemistry I, OGD.

For your convenience, our responses are preceded by your comments.

If you need further information, please contact me at 847-967-5600.

Sincerely,

Kamel F. Egbaria
Vice President, Research and Development

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38. Chemistry Comments to be Provided to the Applicant

AADA/ANDA: 75-260 APPLICANT: Morton Grove Pharmaceuticals, Inc.

DRUG PRODUCT: Tretinoin Topical Solution USP, 0.05%

The deficiencies presented below represent FACSIMILE deficiencies.

A. Deficiencies:

1. The limits for individual and total solvents are acceptable, but your response did not provide the names of solvents to be tested and the validated method to be used. Please discuss with the manufacturer of the drug substance and provide the information described above.
2. Please provide the information regarding method and its validation used for quantitating individual and total impurities of drug substance.
3. You have indicated that the active raw material, tretinoin, MGP Lot # R70173 was qualified as an in-house standard by running all the required tests given in USP 23. The information provided (USP requirement) is not enough for Lot # R70173 to be in-house standard. In addition to ID tests, please provide data showing that Lot # R70173 is comparable to USP reference standard in terms of purity.
4. Please provide up to date room temperature data to support your proposed expiration date. The expiration dating period for the drug product will be based on room temperature stability data since your accelerated stability study was performed without required control of relative humidity.

- B. In addition to responding to the deficiencies presented above, please note and acknowledge that USP methods are the regulatory methods and will prevail in the event of a dispute.

Sincerely yours,


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



May 26, 1998

Via Federal Express

Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, Illinois 60053
Phone (847) 967-5600
Fax (847) 967-2211

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

ORIG AMENDMENT
N/AC

ANDA # 75-260
Tretinoin Topical Solution, USP (Product Code 8151)

**Re: Major Amendment in Response to Deficiency Letter,
Patel, Phillips, and Conner to Bordoni, dated April 29,
1998**

Dear Mr. Sporn:

Pursuant to the Deficiency Letter (copy enclosed) from Rashmikant M. Patel, Jerry Phillips, and Dale Conner, dated April 29, 1998, Morton Grove Pharmaceuticals, Inc., (MGP) is amending the above application. A complete copy of this amendment is being sent to the Chicago District Office, FDA; Rashmikant M. Patel, Ph.D., Director, Division of Chemistry I, OGD; and to Jerry Phillips, Director, Division of Labeling and Program Support, OGD. Because the Division of Bioequivalence has completed its review and has no questions at this time, a copy of this response is not being sent to Dale Conner, Pharm. D., Director of Bioequivalence, OGD.

For your convenience, our responses are preceded by your comments.

If you have any further questions, please call me at 847-967-5600.

Sincerely,

Maurice E. Bordoni
Vice President, Regulatory Affairs

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MAY 29 1998

APR 29 1998

38. Chemistry Comments to be Provided to the Applicant

AADA/ANDA: 75-260 APPLICANT: Morton Grove Pharmaceuticals, Inc.

DRUG PRODUCT: Tretinoin Topical Solution USP, 0.05%

The deficiencies presented below represent MAJOR deficiencies.

A. Deficiencies:

Page(s) 1

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

Chem Comments

4/29/98

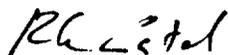
Section 17. Stability of the Finished Dosage Form

24. Stability testing result of the reference listed drug on page 462 indicates that total degradation (%) is not same as the sum of degradant isotretinoin (%) and degradation individual (%). Please explain.
25. Storage conditions for accelerated study for non-aqueous products should include 75% relative humidity. Please provide all available RT data to support your proposed expiration date.
26. The percent of degradant isotretinoin at 3 months shows 1.22 under accelerated condition and 1.55 under room temperature condition. Please explain why the percent value under room temperature is greater than the value under accelerated condition.

27. Please provide a quantitative specification for the color of the product on stability.

B. In addition to responding to the deficiencies presented above, please note and acknowledge that USP methods are the regulatory methods and will prevail in the event of a dispute.

Sincerely yours,



Rashmikant M. Patel, Ph.D.

Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:75-260

APPLICANT:Morton Grove Pharamceuticals, Inc.

DRUG PRODUCT:Tretinoin Topical Solution, USP

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

Please note that the bioequivalency 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 bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,



Dale Conner, Pharm. D.

Director

Division of Bioequivalence

Office of Generic Drugs

Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA:75-260

APPLICANT:Morton Grove Pharamceuticals, Inc.

DRUG PRODUCT:Tretinoin Topical Solution, USP

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

Please note that the bioequivalency 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 bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,



Dale Conner, Pharm. D.

Director

Division of Bioequivalence

Office of Generic Drugs

Center for Drug Evaluation and Research

ANDA 75-260

Morton Grove Pharmaceuticals, Inc.
Attention: Maurice E. Bordoni
6451 West Main Street
Morton Grove, IL 60053

DEC 11 1997

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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.

NAME OF DRUG: Tretinoin Topical Solution USP, 0.05%

DATE OF APPLICATION: November 24, 1997

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 26, 1997

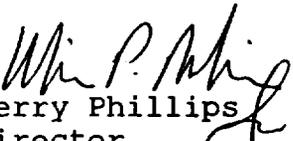
We will correspond with you further after we have had the opportunity to review the application.

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

Should you have questions concerning this application, contact:

Joseph Buccine
Project Manager
(301) 827-5848

Sincerely yours,


Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research



November 24, 1997

Via Federal Express

Morton Grove Pharmaceuticals, Inc.
6451 West Main Street
Morton Grove, Illinois 60053
Phone (847) 967-5600
Fax (847) 967-2211

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

**Re: Tretinoin Topical Solution, USP
(Product Code 8151)
Abbreviated New Drug Application**

Dear Mr. Sporn:

In accordance with Section 505(j) of the Federal Food, Drug, and Cosmetic Act, Morton Grove Pharmaceuticals, Inc., (MGP) submits this abbreviated application for the generic drug product **Tretinoin Topical Solution, USP**. Three copies of the application are being provided: an archival copy, a review copy, and a field copy as required under 21 CFR § 314.94. Each copy consists of two volumes. Each volume of the review copy contains a true and complete copy of the application form required under § 314.94(a)(1) and a copy of the table of contents. In addition, we are providing three additional copies of the methods section.

The field copy, which contains all sections including a copy of the application form required under § 314.94(a)(1), has been submitted to the FDA Chicago District Office on the date of this letter.

On the basis of the data submitted within, we are asking for a waiver of the requirement for the submission of evidence demonstrating bioavailability or

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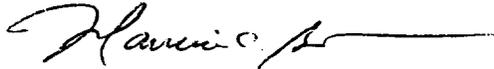
GENERIC DRUGS

bioequivalence for the proposed drug product and an expiration dating period of 24 months for the package size listed in this application. The expected production batch size is _____.

All materials stamped "Confidential" are considered proprietary information and should not be released under the Freedom of Information Act.

Should you require any additional information, please do not hesitate to contact us. Your prompt and thorough attention to this matter is greatly appreciated.

Sincerely,



Maurice E. Bordoni
Vice President, Regulatory Affairs