CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75491

CORRESPONDENCE

ANDA 75-491

Mylan Pharmaceuticals Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

DEC 9 1998

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 the telephone conversation dated November 10, 1998 and your patent amendment dated November 23, 1998.

NAME OF DRUG: Bupropion Hydrochloride Tablets, 75 mg and 100 mg

DATE OF APPLICATION: October 30, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 2, 1998

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:

Tim Ames
Project Manager
(301) 827-5849

Sincerely yours,

/S/

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

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

FAX COVER

DATE: March 22, 2000

TO: Mr. Tim Ames, Project Manager
Division of Chemistry II
OGD, CDER, FDA

FROM: Frank R. Sisto, Vice President
Regulatory Affairs Department
Mylan Pharmaceuticals Inc.

RE: BUPROPION HYDROCHLORIDE TABLETS, 75MG AND 100MG
ANDA #75-491
RESPONSE TO AGENCY CORRESPONDENCE OF FEBRUARY 25, 2000

Dear Mr. Ames:

Following please find a copy of our cover letter for the amendment to the above referenced application which provides for the information requested in a correspondence from the Agency dated February 25, 2000. Hard copy was sent in duplicate to ANDA #75-491 by express mail for delivery on Wednesday, March 22, 2000.

Please contact me if you have any questions or comments.

Sincerely,

Frank R. Sisto

PHONE - (800) 826-9526 Ext. 6600

FAX - (304) 285-6407

Number of pages including this sheet 3

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

FA recd to CMC Reviewer for Review.
3/24/2000

NEW DOCUMENT NC TO FA

MAR 21 2000

Office of Generic Drugs, CDER, FDA
Gary J. Buehler, Acting Director
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

FACSIMILE AMENDMENT
(CMC INFORMATION ENCLOSED)

RE: BUPROPION HYDROCHLORIDE TABLETS, 75MG AND 100MG
ANDA #75-491
RESPONSE TO AGENCY CORRESPONDENCE OF FEBRUARY 25, 2000

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the comments from the Agency pertaining to this application which were provided to Mylan in a facsimile dated February 25, 2000. Reference is also made to a March 20, 2000 telephone conversation between Mr. Tim Ames and Dr. Ubrani Venkataram of your Office and representatives from Mylan in which we discussed Comment 2 from the February 25, 2000 letter. A copy of the February 25 correspondence is provided in Attachment G. In response to the Agency's February 25 comments and our discussion of March 20, Mylan wishes to amend this application as follows.

FDA COMMENT 1. We find that it has not been adequately demonstrated that the analytical method for analysis of the drug product is stability indicating. Forced degradation study should be repeated on samples of the drug product stressed under strong acid, strong base, and oxidative media in order to evaluate potential excipient interaction or degradation. Please refer to the Stability Guidance (February 1987).

MYLAN RESPONSE: As requested, Mylan has performed an intentional degradation study on drug product samples stressed under strong acid, strong base, and oxidative media. The study is provided in Attachment A and demonstrates that the methods are stability-indicating and no interferences occur from excipients or degradation products.

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
MAR 22 2000
OGD

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Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

FDA COMMENT 2. Please include a test and provide specifications for moisture content of the coated tablets as an in-process control.

MYLAN RESPONSE:

Furthermore, Mylan is also tightening the moisture specification for the finished product from Not More Than % to Not More Than %. The revised finished product specifications, Loss on Drying procedure, and post-approval stability protocols are provided in Attachments D, E and F, respectively.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Marilyn A. Friedag for

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

NOV 23 1998

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

NEW CORRESP

PATENT AMENDMENT

RE: Bupropion Hydrochloride Tablets, 75mg and 100mg
ANDA #75-491

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above and to November 11 and 17, 1998 telephone calls with the Agency's Mr. Gregory Davis regarding this application.

Mylan acknowledges Mr. Davis' request for a change in patent certification. This change is based on the deletion of unacceptable patents for this product, as indicated in the Electronic Orange Book on the Center for Drug Evaluation and Research web site (www.fda.gov/cder/ob). As such, please find enclosed a certification identifying 'no relevant patents' as a replacement for the originally submitted Paragraph IV Certification. A copy of the corresponding Electronic Orange Book section is included in support of this revision.

In addition, Mylan would like to take this opportunity to correct a typographical error found in the 'Form 356h - Establishment Information' section of the original submission. This error has been corrected and the revised page (page 4A) is provided as a replacement for page 4 of the original application.

Should you have any further questions regarding this amendment, please contact the undersigned by phone at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

enclosures

cc: Mr. Gregory Davis via facsimile

RECEIVED
NOV 24 1998
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MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

OCT 30 1998

labeling reviewer drafted 12/22/98 a Vezza

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

ELECTRONIC DATA ENCLOSED
BIOEQUIVALENCE DATA ENCLOSED

RE: BUPROPION HYDROCHLORIDE TABLETS, 75MG AND 100MG

Dear Mr. Sporn:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.92 and 314.94, we submit the enclosed abbreviated new drug application for:

Proprietary Name: None
Established Name: Bupropion Hydrochloride Tablets
This application consists of a total of 19 volumes.
- Archival Copy - 8 volumes.
- Review Copy - 9 volumes.
  - Technical Section For Chemistry - 3 volumes.
  - Technical Section For Pharmacokinetics - 6 volumes.
- Analytical Methods - 2 extra copies; 1 volume each.

NOTE: The Technical Section for Pharmacokinetics of the review copy and the archival copy each contain a data diskette for the bioequivalence study conducted in support of this application.

This application provides for the manufacture of Bupropion Hydrochloride Tablets, 75mg and 100mg. Except for the preparation of one manufacturing intermediate all operations in the manufacture, packaging, and labeling of the drug product will be performed by Mylan Pharmaceuticals Inc., 781 Chestnut Ridge Road, Morgantown, WV 26505-2730.

As required by 21 CFR 314.94(d)(5) we certify that a true copy of the technical sections of this application, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office. The following Table of Contents and Reader's Guide detail the documentation submitted in support of this application.

All correspondence regarding this application should be directed to the attention of the undersigned at Mylan Pharmaceuticals Inc., P.O. Box 4310, 781 Chestnut Ridge Road, Morgantown WV, 26504-4310, or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/tlr

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NOV 0 2 1998
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Purchasing (304) 598-5401
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labeling review drafted 8/27/99 AVegin

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

AUG 16 1999

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

NDA ORIG AMENDMENT
MAC

MAJOR AMENDMENT
(CMC AND LABELING INFORMATION ENCLOSED)

RE: BUPROPION HYDROCHLORIDE TABLETS, 75MG AND 100MG
ANDA #75-491
RESPONSE TO AGENCY CORRESPONDENCE DATED JUNE 28, 1999

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the comments from the Agency pertaining to this application which were provided to Mylan in a facsimile dated June 28, 1999. In response to the Agency's June 28 comments, Mylan wishes to amend this application as follows.

A. REGARDING CHEMISTRY ISSUES

The following comments pertain to your raw material controls:

FDA COMMENT 1. It is recommended that you include a test for Bulk Density and Tapped Density in your drug substance testing specifications.

MYLAN RESPONSE: Mylan Pharmaceuticals acknowledges the reviewer's recommendation for the addition of a test for Bulk Density and Tapped Density in Mylan's drug substance specification and agrees to include a specification for Tapped Density according to USP 23 <616> Bulk Density and Tapped Density. A Tapped Density specification limit between g/mL has been established. Mylan has proposed a Tapped Density method, rather than a Bulk "Poured" Density, to allow for a more rugged determination of this attribute. A revised drug substance specification and certificate of analysis are included in Attachment A.

FDA COMMENT 2. Certificate of Analysis for Bupropion Hydrochloride drug substance (page 2453) showed either very small amounts of the known related compounds or none detected. It is recommended that you tighten these specifications.

MYLAN RESPONSE: Mylan Pharmaceuticals acknowledges the reviewer's request to revise the specifications for the known related compounds and agrees to lower each limit of the four known impurities from NMT % to NMT %. The revised specification and Certificate of Analysis are provided in Attachment A. The revised test method is included in Attachment B.

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REC'D
AUG 17 1999
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Department—Fax Numbers
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FDA COMMENT 3. Please include the testing specification for which appears on your COA on page 2453 to the testing specifications for Bupropion Hydrochloride for future commercial production batches (page 2450).

MYLAN RESPONSE: The drug substance specification for Bupropion Hydrochloride which included was provided in the original application on page 3221. A prior version of the specification was inadvertently included on page 2450.

The revised specification for Bupropion Hydrochloride which encompasses the testing specification for as well as revisions in response to additional agency comments, has been provided in this amendment under Attachment A.

FDA COMMENT 4. Please provide COA for the Microcrystalline Cellulose (supplier lot #9806491).

MYLAN RESPONSE: In this instance, did not generate a Certificate of Analysis for the Microcrystalline Cellulose (Lot #9806491). The material was evaluated by Mylan and conformed to established specifications as demonstrated by Mylan's Certificate of Analysis provided on page 2570 of the original submission.

For all future production batches, will provide Mylan with a Certificate of Analysis for each lot produced. In addition, Mylan will continue to evaluate and release the material based upon compliance to the current specifications as outlined on page 2569 of the original submission.

FDA COMMENT 5. The mixing time on page 2837 is reported as minutes for Part I-A Solution Manufacture Instructions whereas for Part II-A (page 2841) and Part III-A (page 2845) is reported as minutes and minutes respectively. Please clarify the difference in mixing times.

MYLAN RESPONSE: The Hydrochloric Acid and the Purified Water used in the manufacture of the Part I-A, Part II-A, and Part III-A solutions are completely miscible liquids. Therefore, a homogeneous solution should be achieved within the minimum minute mixing time designated in the batch record, and the homogeneity of the solution is maintained during prolonged mixing.

Solutions are prepared prior to use and it is not atypical for operators to perform other batch related tasks while solutions are mixing. All solution sub-parts have met the minimum five (5) minute mixing time requirement and the actual mixing times have been recorded in the batch record.

FDA COMMENT 6. Please provide more information on poly-liners, used for storage of intermediate.

MYLAN RESPONSE: The polyethylene liners used for storage of the intermediate will be tested and released by Mylan prior to use according to the established specifications and supplied to . . Specifications and representative Certificates of Analysis for the liners are provided in Attachment C.

FDA COMMENT 7. Please provide bottle manufacturer's testing data and specifications for container resins.

MYLAN RESPONSE: The requested information regarding the bottle manufacturers' testing data and specifications for container resins is considered confidential and proprietary in nature as indicated in the correspondence provided in Attachment D. As such, the information can be found in the manufacturers' respective Drug Master Files:

Container	DMF
Container	DMF
Container	DMF
Resin	DMF
Resin	DMF

The appropriate authorization letters can be found on pages 3123-3133 of the original submission.

FDA COMMENT 8. Please provide closure manufacturer's testing data and specifications for closure resins.

MYLAN RESPONSE: The requested information regarding the closure manufacturer's testing data and specifications for closure resins is considered confidential and proprietary in nature as indicated in the correspondence provided in Attachment E. As such, the information can be found in the manufacturers' respective Drug Master Files:

Closure	DMF
Closure	DMF
Resin	DMF
Resin	DMF
Resin	DMF

The appropriate authorization letters can be found on pages 3135-3143 of the original submission.

FDA COMMENT 9. It is recommended that you include the as an in-process control in the master production records. Please revise and resubmit appropriate documents, include sampling and specifications. It is recommended that samples be drawn either from the blender or drums (more than six samples) and the sample size should not be more than 1-3 dosage units. acceptance criteria of 90.0% - 110% (mean of individual test results) with relative standard deviation (RSD) of NMT % is recommended.

MYLAN RESPONSE: Mylan will routinely perform testing on the final blend prior to its release for compression. Final blend samples will be collected at specified locations from the blender or drums (more than six samples) and each sample will represent 1 to 3 dosage units. As requested, the in-process final blend specifications have been revised to incorporate the acceptance criteria of % (mean of individual values) with an RSD of NMT % and are provided in Attachment F.

Bupropion Hydrochloride Tablets, 75mg and 100mg production master batch records include a quality control sampling step (page 9, to control the in-process sampling and testing of the final blend. Additionally, the production master batch records include a required Quality Control release for compression (page 11 of each production master batch record). Continuation of the manufacturing process is contingent upon the release of the final blend from Quality Control if found to be in compliance with the established in-process specification sheet associated with this stage of production. Therefore, in-process specifications are not included with the actual batch record.

FDA COMMENT 10. On page 3035 and page 3036 you have included test results for the bulk final blend samples for each strength. The results actually do fall in the recommended acceptance criteria above. Please provide the actual sample size which was used for

MYLAN RESPONSE: The actual sample sizes used to produce the test results on page 3035 and 3036 are as follows:

Bupropion Hydrochloride Tablets, 75 mg
Lot # 2E001B

Blender Location	Sample Size
Top Left	mg
Top Center Left	mg
Top Center	mg
Top Center Right	mg
Top Right	mg
Middle Left	mg
Middle Center	mg
Middle Right	mg
Bottom Left	mg
Bottom Right	mg

MYLAN RESPONSE: **Bupropion Hydrochloride Tablets, 100 mg**
(Continued) **Lot # 2E002B**

Blender Location	Sample Size
Top Left	mg
Top Center Left	mg
Top Center	mg
Top Center Right	mg
Top Right	mg
Middle Left	mg
Middle Right	mg
Bottom Left	mg
Bottom Right	mg

FDA COMMENT 11. Please set a target for tablet hardness and tablet thickness.

MYLAN RESPONSE: Mylan has validated a hardness range of kg for Bupropion Hydrochloride Tablets, 75mg and a hardness range of kg for Bupropion Hydrochloride Tablets, 100mg. This validation was based on multi-point dissolution and physical test data found in the original submission on pages 2829-2830. The tablet press will be set-up to utilize a target range of kg for the 75mg tablets, which is the approximate hardness range within which the exhibit batch was compressed. For 100mg tablets, the tablet press will be set-up to utilize a target range of kg, which is the approximate hardness range within which the exhibit batch was compressed. If necessary, this target range may be adjusted within the validated range once sufficient data is accumulated.

The tablet thickness value is reliant upon the tablet hardness, and the hardness target will dictate the thickness of the tablet. Based on the hardness and thickness results observed during validation of the exhibit batch, the predicted average thickness for the 75mg tablets is expected to be which falls between the specified range of The predicted average thickness for the 100mg tablets is expected to be " which falls between the specified range of

FDA COMMENT 12. The proposed weight gain range for Coated Tablet Specifications are wide. Please tighten these limits.

MYLAN RESPONSE: For both the 75mg and the 100mg tablet strengths, Mylan has set the target cosmetic color coat weight gain at % of the core tablet weight with a range of % in order to consistently manufacture a pharmaceutically elegant dosage form. The proposed target weight gain range is based upon SUPAC Level 1 acceptance guidelines for film coating which are changes unlikely to impact formulation quality and performance. In addition, dissolution profiles for core and coated tablets provided on pages 3049-3052 of the original submission confirm that the film coating does not alter drug release from the dosage form.

FDA COMMENT 13. Accelerated stability studies on pages 3467-3479 showed either very small amounts of the known related compounds or none detected. It is recommended that you further tighten these specifications for the final product specifications at release and stability.

MYLAN RESPONSE: As requested, Mylan has tightened the related compounds specifications for the known impurities in the drug product from Not More Than % to Not More Than % at release and stability. The revised procedure, finished product specifications, and post-approval stability protocols are provided in Attachment G.

FDA COMMENT 14. Please include identification tests in your Microcrystalline Cellulose specifications.

MYLAN RESPONSE: Subsequent to initial release, a test for identification was added to the Microcrystalline Cellulose specifications as noted on page 2568 of the original submission. The revised specification and Certificate of Analysis for the material used in the exhibit batch, inclusive of the identification test, were provided in the original submission on pages 2569-2570.

FDA COMMENT 15. It is recommended that you stress the Bupropion Hydrochloride Tablets under strong acid, strong base and oxidation conditions to investigate the stability-indicating properties of the Assay and Related Compounds procedure.

MYLAN RESPONSE: Mylan acknowledges the utility of strong acid, strong base and oxidation conditions in establishing the stability-indicating properties of the Assay and Related Compounds procedures. Samples of Bupropion Hydrochloride drug substance were subjected to these solution-phase stress conditions and tested using the Assay and Related Compounds methods, in accordance with the November 1994 Reviewer Guidance for Validation of Chromatographic Methods. The specificity/selectivity section of this guidance specifies that these solution-phase stress conditions are recommended for the drug substance only. Mylan has further demonstrated the stability-indicating properties of the methods by solid-state environmental stress testing (extreme heat, moderate heat/high humidity, and intense light) of the drug product and excipients. Mylan believes that, in conjunction, these studies are sufficient to demonstrate the stability-indicating properties of the Assay and Related Compounds methods for Bupropion Hydrochloride Tablets.

B. REGARDING MISCELLANEOUS ISSUES

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

FDA COMMENT 1. The referenced DMF is deficient and the deficiency has been communicated to the DMF holder.

MYLAN RESPONSE: Mylan acknowledges that Drug Master File (DMF) for Bupropion Hydrochloride was reviewed and found deficient. Enclosed in Attachment H is a copy of a cover letter from indicating that a response to the DMF deficiency letter has been forwarded to the FDA.

FDA COMMENT 2. The Establishment Evaluation Request (EER) is pending.

MYLAN RESPONSE: Mylan acknowledges that the Establishment Evaluation Request (EER) is pending.

FDA COMMENT 3. Your Method Validation package is being sent to our Philadelphia District Laboratory.

MYLAN RESPONSE: Mylan acknowledges that our Method Validation package is being sent to the Philadelphia District Laboratory. As per agency policy, Mylan commits to resolving any issues identified in the Method Validation process subsequent to approval.

C. REGARDING LABELING ISSUES

MYLAN RESPONSE: Regarding the labeling deficiencies, Attachment L contains twelve (12) copies of the following final printed bottle labels, outsert and patient leaflet for Bupropion Hydrochloride Tablets, 75mg and 100mg:

BOTTLE LABELS

75mg
Code RM0433A - Bottles of 100 Tablets
Code RM0433B - Bottles of 500 Tablets

100mg
Code RM0435A - Bottles of 100 Tablets
Code RM0435B - Bottles of 500 Tablets

OUTSERT

Code BUPR:R1, Revised June 1999

The enclosed labeling incorporates the revisions requested in the Agency's letter of June 28, 1999. A copy of this correspondence is provided in Attachment I for the convenience of the reviewer.

In order to facilitate the review of this labeling, Attachment J contains a side-by-side comparison of the final printed labels to those previously submitted and Attachment K contains a side-by-side comparison of the final printed outsert (BUPR:R1) to the outsert that was previously submitted. It is noted that prior to approval of this application, the agency reserves the right to request further changes in the Mylan labeling based upon the changes in the approved labeling of the listed drug or upon further review of the application.

Pursuant to 21 CFR 314.96(b), we certify that a true copy of the technical sections of this amendment, as submitted to the Office of Generic Drugs, has been forwarded to the FDA's Baltimore District Office.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

February 18, 2000

NDA ORIG AMENDMENT
N/A

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

FACSIMILE BIOEQUIVALENCE AMENDMENT

RE: BUPROPION HYDROCHLORIDE TABLETS, 75MG AND 100MG
ANDA #75-491
RESPONSE TO AGENCY CORRESPONDENCE OF FEBRUARY 18, 2000

Dear Mr. Sporn:

Reference is made to the pending Abbreviated New Drug Application (ANDA) identified above, which is currently under review, and to a February 18, 2000 facsimile from the Agency requesting additional long term frozen stability for the bupropion hydrochloride bioequivalence study (BUPR-9764). In response to the February 18 facsimile, Mylan wishes to amend this application with updated long term frozen stability. An addendum to the analytical assay validation report is provided in Attachment 1. The addendum provides long term stability for bupropion, hydroxybupropion and threohydrobupropion in plasma stored at -70°C for 175 days. A copy of the Agency's February 18 facsimile is provided in Attachment 2.

This amendment is submitted in duplicate. Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

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ALTANA

Altana Inc. 60 Baylis Road, Melville, N.Y. 11747 631-454-7677

April 25, 2001

NC to FAX

NEW CORRESP

Dr. Paul Schwartz
Office of Generic Drugs
Center for Drug Evaluation and Research
Food, and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: ANDA 75-276 **TELEPHONE AMENDMENT**
Betamethasone Dipropionate Gel, 0.05% (Augmented)

Dear Dr. Schwartz:

Reference is made to the Altana Inc. Abbreviated New Drug Application submitted on December 18, 1997 for Betamethasone Dipropionate Gel, 0.05% (Augmented) in accordance with Section 505 (j) of the Federal Food, Drug and Cosmetic Act. Reference is also made to our amendments of November 15, 1999, November 3, 2000 and April 20, 2001.

Reference is also made to telephone conversations of April 23, 2001 and April 24, 2001 between members of the office and Altana Inc. These discussions concerned degradation issues, stability specifications, and identification of the peak at Relative Retention Time of approximately

Degradation issue:

As we discussed, in Attachment 14 of our November 15, 1999 amendment data was submitted showing a comparison of three of our lots vs. Schering's product, which were stored for 18 months at the Controlled Room Temperature stability conditions of 25°C/60% RH. The data for Schering's product is in line with Altana's Inc. three batches, i.e. total degradation of % (Schering) vs. a range of % (Altana). Schering's lot was tested September 1, 1998, and the expiration date was October 1998.

Stability specifications:

Altana has revised the stability specifications for degradation products as follows:

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APR 2 6 2001
OGD

	Current spec.
Betamethasone	not more than %
Relative retention time of approximately	not more than %
Others	each not more than %
Total	not more than %

	Revised spec.	
Betamethasone	not more than	%
Relative retention time of approximately 0.43 (betamethasone17-propionate)	not more than	%
Relative retention of approximately 0.50 (betamethasone 21-propionate)	not more than	%
Others	not more than	%
Total	not more than	%

The revised specifications are included as Attachment 1.

Identification of peak at RRT of approximately

The peak has been identified as betamethasone 21-propionate. This information was included in Attachment 3, page 5 of the April 20, 2001 amendment. This page is included in Attachment 2 for ease of review.

This concludes Altana's response to this Telephone Amendment. If you have any questions, or require any additional clarifications, please contact me at (631) 454-7677 ext. 2091. Fax communication may be made to (631) 756-5114.

Sincerely,
ALTANA INC.

Virginia Carman
Associate Director, Regulatory Affairs

VC/cc