CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 40-298

CORRESPONDENCE

ANDA 40-298

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

MAR 17 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 also made to the telephone conversation dated March 9, 1998 and your correspondence dated March 10, 1998.

NAME OF DRUG: Extended Phenytoin Sodium Capsules USP, 100 mg

DATE OF APPLICATION: February 27, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: March 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:

Kassandra Sherrod
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

SEP 28 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

FA

BIOEQUIVALENCE AMENDMENT
(CMC DATA ENCLOSED)

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY CORRESPONDENCE DATED SEPTEMBER 22, 1998

Dear Mr. Sporn:

Reference is made to the ANDA identified above, which is currently under review, and to the September 22, 1998 correspondence pertaining to this application which was forwarded to Mylan from the Office of Generic Drugs' Division of Bioequivalence. In response to the September 22 correspondence, Mylan wishes to amend the application as follows:

A. REGARDING BIOEQUIVALENCE ISSUES:

FDA COMMENT 1. The Division of Bioequivalence has completed its review and has no further questions at this time.

The dissolution testing will need to be incorporated into your stability and quality control programs as specified in U.S.P. 23, eighth supplement.

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.

MYLAN RESPONSE: The dissolution testing requested by the Division of Bioequivalence will be incorporated into Mylan's stability and quality control programs as of the date of this amendment. Mylan has revised the finished product specifications and dissolution procedure for Extended Phenytoin Sodium Capsules, USP 100mg to incorporate the requested changes. These revised documents are provided in Attachments A and B, respectively.

SEP 29 1998

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

It is also acknowledged and understood that the bioequivalency comments expressed in the letter dated September 22, 1998 are preliminary and may be revised after review of the entire application.

For your reference, a copy of the September 22, 1998 Agency correspondence is provided in Attachment C. Responses to the chemistry comments contained in the September 22 correspondence along with revised labeling, as requested by the Agency, are being forwarded in a separate amendment to this 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/tlr

enclosures

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

SEP 28 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

FA
NDA ORIG AMENDMENT

FACSIMILE AMENDMENT

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY CORRESPONDENCE DATED SEPTEMBER 22, 1998

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 September 22, 1998. In response to the Agency's facsimile comments of September 22, Mylan wishes to amend this application as follows.

A. **REGARDING CHEMISTRY ISSUES**

Page(s) 2

Contain Trade Secret,

Commercial/Confidential

Information and are not

releasable.

B. REGARDING MISCELLANEOUS ISSUES

FDA COMMENT 1. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

In the compression instructions and parameters for the batch No. R&D 1437, for ablets presented, it is noted that except for the specifications for tablet weight, no hardness, thickness or friability specifications are included. They should. We acknowledge that they are presented in the body of the application.

MYLAN RESPONSE: Mylan's batch records are designed to provide instructions for the actual manufacture of the drug product with in-process specifications for hardness, thickness and friability being provided as separate auxiliary documents. Hardness and thickness are measured throughout the manufacturing process. A composite sample representative of the batch is also tested for hardness thickness and friability. These data are recorded, reviewed and approved by Quality Assurance prior to release of every batch for further processing. If hardness, thickness and/or friability do not meet the established in-process specifications, the product will be rejected by Quality Assurance. Upon completion of the manufacturing and testing of the batch these documents are then included in the batch record file.

C. REGARDING LABELING ISSUES

MYLAN RESPONSE: Attachment E contains twelve (12) copies of the following final printed bottle labels and outsert for Extended Phenytoin Sodium Capsules, USP 100mg:

BOTTLE LABELS
Code RM1560A - Bottles of 100 Capsules
Code RM1560C - Bottles of 1000 Capsules

OUTSERT
Code PHNY:R1 , Revised September 1998

The enclosed labeling incorporates the revisions requested in the Agency's letter of September 22, 1998. A copy of this letter is provided in Attachment B for the convenience of the reviewer.

In order to facilitate the review of this labeling, Attachment C contains a side-by-side comparison of the final printed bottle labels to those previously submitted and Attachment D contains a side-by-side comparison of the final printed outsert (PHNY: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.

As previously noted, a copy of the Agency correspondence dated September 22, 1998 is included in Attachment B, for the convenience of the reviewer. Mylan's response to the comments from the Division of Bioequivalence contained in the September 22, 1998 correspondence are being forwarded in a separate amendment to this application.

Pursuant to 21 CFR 314.96(b), we certify that a true copy 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/tlr

enclosures

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

MAR 10 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

TELEPHONE AMENDMENT
(CMC INFORMATION)

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY TELEPHONE CALL OF MARCH 09, 1998

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above and to the Agency's March 09, 1998 telephone call. Pursuant to the Agency's request, Mylan wishes to amend this application to provide for a reduced finished product production batch size of es. In accordance with OGD's Policy and Procedure Guide #22-90, sule batch size is equivalent to 10X of the apsules obtained during manufacture of the exhibit batch. The revised master production batch records are included in this amendment.

It should be noted that in the original application, the master production batch record for capsules was formatted as a contiguous batch record which included the manufacture of the and the finished dosage form. The revised master production batch records submitted in this amendment for the es batch size are non-contiguous and provide for the manufacture of the ts, and the finished dosage form separately which more closely reflects the manner in which the bioequivalence batch was manufactured. In addition to the production batch records, the "Overview of Manufacturing and Processing Instructions", the "Processing Schemes", and the "Summary Table of Differences" have been revised to provide for the reduction in batch size. Based on the number of pages affected by the revision, we have chosen to replace Section XI: Manufacturing and Processing Instructions, in its entirety (pp. 1780-1859 of the original application) with the enclosed revised version of Section XI for the convenience of the reviewer.

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

RECEIVED
MAR 11 1998
GENERIC DRUGS

R:\ANDA\PHENYTOIN-NA-ER-CAPS\AGENCY-CALL-DATED-03_09_98

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
Business Development	(304) 599-7284	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

This amendment is submitted in duplicate. An additional desk copy is included in this amendment to the attention of Greg Davis. Should you require additional information or have any questions regarding this amendment, please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Laura Deiriggi/for

Frank Sisto
Executive Director
Regulatory Affairs

FRS/tlm

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cc: desk copy to Greg Davis

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

FEB 27 1998

ELECTRONIC DATA ENCLOSED
BIOEQUIVALENCE DATA ENCLOSED

505(j) DOCK
3/11/98
Gregory S. Davis

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

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG

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: Extended Phenytoin Sodium Capsules, USP
This application consists of a total of 15 volumes.
- Archival Copy - 6 volumes.
- Review Copy - 7 volumes.
  - Technical Section For Chemistry - 3 volumes.
  - Technical Section For Pharmacokinetics - 4 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.

This application provides for the manufacture of Extended Phenytoin Sodium Capsules, USP 100 mg. All operations in the manufacture, packaging, and labeling of the drug product are 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 Reader's Guide and Table of Contents 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.

Sincerely,

F.M. Sisto FOL

Frank R. Sisto
Executive Director
Regulatory Affairs

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MAR 0 2 1998
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FRS/tlm

Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
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Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
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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

JUN 25 1998

NDA ORIG AMENDMENT
B

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

TELEPHONE AMENDMENT
(BIOEQUIVALENCE INFORMATION)

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY TELEPHONE CALL OF JUNE 23, 1998

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above and to the Agency's June 23, 1998 telephone call. Pursuant to the Agency's request, Mylan wishes to amend this application to provide data demonstrating the recovery of the internal standard used in the phenytoin analytical procedure for the bioequivalence study submitted in the referenced ANDA.

Internal standard recovery was not a required test procedure at the time the fasting (PHEN-9734) bioequivalence study was submitted. However, recovery of internal standard was investigated as part of the methods development for the analytical procedure. The following summarizes the results of this experiment:

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

Sincerely,

Frank Sisto
Vice President
Regulatory Affairs

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JUN 26 1998
GENERIC DRUGS

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Department Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
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Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

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

December 15, 1998

FA

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

TELEPHONE AMENDMENT

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY TELEPHONE CALL OF DECEMBER 14, 1998

Dear Mr. Sporn:

Reference is made to the Abbreviated New Drug Application identified above, which is currently pending approval, and to a December 14, 1998 teleconference regarding this application which took place between representatives from Mylan and the Office of Generic Drugs. As a result of the discussions which took place during the teleconference, Mylan wishes to amend this application with the following additional information:

With regard to item 1, Mylan has revised the in-process controls

are provided in Attachments A and B, respectively.

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DEC 16 1998

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
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Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

The enclosed Table of Contents details the documentation submitted in support of this amendment.

Pursuant to 21 CFR 314.96(b) we certify that a true copy 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 have any questions regarding this amendment, please contact the undersigned by telephone at (304) 599-2595, ext. 6600 or by facsimile at (304) 285-6407.

Sincerely,

Frank Sisto
Vice President
Regulatory Affairs

FRS/tlr

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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

ORIG AMENDMENT
N/FA

December 9, 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

TELEPHONE AMENDMENT

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY TELEPHONE CALL OF DECEMBER 9, 1998

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above and to a December 9, 1998 telephone call with Dr. Florence Fang.

Pursuant to the Agency's request, Mylan wishes to amend this application to provide a revised quantitative composition statement which encompasses all product components.

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

Sincerely,

Marilyn A. Friedly/for

Frank Sisto
Vice President
Regulatory Affairs

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DEC 10 1998
Pending Desk

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Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
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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

ORIG AMENDMENT
N/FA

November 20, 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

TELEPHONE AMENDMENT

RE: EXTENDED PHENYTOIN SODIUM CAPSULES, USP 100 MG
ANDA 40-298
RESPONSE TO AGENCY TELEPHONE CALL OF NOVEMBER 20, 1998

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above and to a November 20, 1998 telephone call with Dr. Florence Fang.

Pursuant to the Agency's request, Mylan wishes to amend this application to provide a revised quantitative composition statement which encompasses all product components.

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

Sincerely,

Frank Sisto
Vice President
Regulatory Affairs

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NOV 23 1998
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Department—Fax Numbers		Information Systems	(304) 285-6404	Purchasing	(304) 598-5401
Accounting	(304) 285-6403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 285-6409
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