CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74910

CORRESPONDENCE

ANDA 74-910

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

AUG 9 [illegible]

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: Diltiazem Hydrochloride Extended-release Capsules USP, 60 mg, 90 mg, and 120 mg

DATE OF APPLICATION: June 12, 1996

DATE OF RECEIPT: June 13, 1996

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) 594-0305

Sincerely yours,

/S/ 8/9/96

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

ANDA 74-910
cc: DUP/Jacket
Division File
Field Copy
HFD-600/Reading File
HFD-82
HFD-615/MBennett

Endorsement: HFD-615/PRickman, Chief, RSB /S/ 8/6/96 date
HFD-615, AMWeikel, CSO /S/ 8/9/96 date
HFD-647, JSimmons,Sup. Chem. /S/ [illegible] date

ANDA Acknowledgement Letter!

ANDA 74-910

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

DEC 27 1996

Dear Sir:

This is in reference to your abbreviated new drug application dated June 12, 1996, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Diltiazem Hydrochloride Extended-Release Capsules USP (Twice-a-Day-Dosage), 60 mg, 90 mg, and 120 mg.

The application is deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

A. Chemistry Deficiencies:

B. LABELING DEFICIENCIES

1. GENERAL COMMENT:

Revise so that the phrase, "Twice-a-Day dosage" follows the established name of your product as below, where it appears on container labels and package insert labeling:

Diltiazem Hydrochloride Extended-release Capsules USP (Twice-a-Day Dosage)

2. CONTAINER

a. See GENERAL comment.

b. Please include the following statement on the container label:

Diltiazem Hydrochloride Extended-release Capsules USP which exhibit different pharmacokinetics are also marketed. Please confirm you are dispensing the prescribed formulation.

c. Revise your definition of controlled room temperature to be consistent with that appearing in the HOW SUPPLIED section of your package insert.

3. INSERT

a. CLINICAL PHARMACOLOGY

I. Mechanism of Action

Make the following revision in the first sentence, "Diltiazem hydrochloride produces its...". (note singular subsection heading)

ii. Hemodynamic and Electrophysiologic Effects

Penultimate paragraph

Intravenous diltiazem hydrochloride...

iii. Pharmacokinetics and Metabolism (Last sentence)

...study in nine patients...

iv. Last paragraph

a) Heading - See GENERAL comment.

b) Delete the first sentence.

b. INDICATIONS AND USAGE

...Capsules USP (Twice-a-Day Dosage)...hypertension. They may...

c. WARNINGS (Cardiac Conduction)

Make the following revision to the last sentence of the first paragraph, "...of diltiazem. (See ADVERSE REACTIONS)".

d. PRECAUTIONS

I. Drug Interactions - Beta Blockers

Second paragraph, "...of diltiazem hydrochloride...".

ii. Pregnancy: Teratogenic Effects - Pregnancy Category C

Revise this subsection heading as above.

iii. Pediatric Use

...in pediatric patients...

e. ADVERSE REACTIONS (Other - second paragraph)

I. Make the following revisions in the first sentence:

...diltiazem: allergic reactions, alopecia, angioedema (including facial or periorbital edema), asystole, erythema multiforme (including Stevens-Johnson syndrome, toxic epidermal necrolysis), extrapyramidal...

ii. Make the following revision in the penultimate sentence, "...generalized rash, some characterized...".

f. OVERDOSAGE OR EXAGGERATED RESPONSE

I. Add the following sentence as the penultimate sentence of the sixth paragraph:

Limited data suggest that plasmapheresis or charcoal hemoperfusion may hasten diltiazem elimination following overdose.

ii. Make the following revision in the penultimate sentence, "...or norepinephrine bitartrate...".

g. DOSAGE AND ADMINISTRATION

Make the following revision in the second sentence, "...therefore, dosage adjustments...".

h. HOW SUPPLIED

I. Include the established name of the product in this section, e.g., Diltiazem hydrochloride extended-release capsules (twice-a-day dosage) are supplied as follows:

ii. We encourage the inclusion of the statement appearing under CONTAINER (b) in this section.

Please prepare and submit final print container labels and final printed (or printers proof) package insert labeling. Please note that final printed insert labeling is not required for tentative approval of an application if it is granted with more than 90 days remaining from the date when full approval can be considered. We will accept final "printers proof" for the insert only.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon further changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

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. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered to represent a MINOR AMENDMENT and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 12/26/96

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 74-910

Mylan Pharmaceuticals Inc.
Attention: Frank R. Sisto
781 Chestnut Ridge road
P.O. BOX 4310
Morgantown WV 26504-4310

OCT 31 1996

Dear Sir:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Diltiazem Hydrochloride Extended-release Capsules 60 mg, 90 mg and 120 mg.

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

2. The following interim dissolution testing will need to be incorporated into your stability and quality control programs:

   The dissolution testing should be conducted in 900 mL of water at 37°C using USP 23 Apparatus 2 (Paddle) at 100 rpm. The test product should meet the following specifications:

4 hrs		%
8 hrs		%
12 hrs		%
24 hrs	NLT	%

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

/S/

Rabindra Patnaik, Ph.D.
Acting Director, Division of Bioequivalence
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

BIOAVAILABILITY

NEW CORRESP

SEP 12 1996

RECEIVED

SEP 13 1996

GENERIC DRUGS

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: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES,USP
60 MG, 90 MG AND 120 MG
ANDA 74-910
BIO TELEPHONE AMENDMENT PER
SEPTEMBER 11, 1996 CONVERSATION WITH DR. MOO PARK

Dear Mr. Sporn:

Reference is made to the pending ANDA identified above for Diltiazem Hydrochloride Extended Release Capsules, 60 mg, 90 mg and 120 mg, and to the September 11, 1996, telephone conversation which took place between Mylan and OGD's Division of Bioequivalence.

During the September 11 telephone conversation, Mylan was requested to provide information pertaining to the analytical validation report for the bioequivalence studies submitted in the Diltiazem ANDA. Specifically we were asked to provide the storage conditions for stock solution stability and the spiked concentration of the processed sample stability samples. Stock solutions for stability determinations were stored at 4°C. The processed sample stability samples were spiked at the middle control level for the standard curve: 25 ng/mL for diltiazem, 25 ng/mL for desmethyldiltiazem, and 12.5 ng/mL for desacetyldiltiazem.

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

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

Department—Fax Numbers					
Accounting	(304) 598-5403	Information Systems	(304) 598-5404	Purchasing	(304) 598-5401
Administration	(304) 599-7284	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Business Development	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 598-5409
Human Resources	(304) 598-5406	Maintenance & Engineering	(304) 598-5411	Sales & Marketing	(304) 598-3232
		Medical Unit	(304) 598-5445		

[RDLIB.ANDA.DILTIAZEM-ER]TELEPHONE-AMENDMENT.091196

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

August 13, 1996

RECEIVED
AUG 2 1 1996
GENERIC DRUGS

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: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES USP 60MG, 90MG AND 120MG
ANDA NO. 74-910

Dear Mr. Sporn:

Mylan hereby amends this application with the attached "Paragraph IV" certification and the following certification of notice to the holders of the patent and the approved application.

Pursuant to Section 505(j)(2)(B)(i) of the Federal Food, Drug and Cosmetic Act and 21 CFR 314.95(d), Mylan certifies it has, concurrently with the filing of this amendment, provided notice to each owner of the patent which is the subject of the certification, or their representatives, and also to the holder of the approved application for the listed drug claimed by said patent. Said notice complies with the requirements set forth in 21 CFR 314.95(c) with respect to the content of the notice.

Further, Mylan commits to amend this application pursuant to 21 CFR 314.95(e) to provide certification that notifications sent to the patent owner and application holder have been received.

Sincerely,

Dawn J. Beto, Esq.
Senior Counsel

DJB/dc

Department—Fax Numbers
Accounting (304) 598-5403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 598-5404
Label Control (800) 848-0463
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Medical Unit (304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 598-5409
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

August 13, 1996

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: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES USP 60MG, 90MG AND 120MG
PATENT NO. 4,721,619
PARAGRAPH IV CERTIFICATION
ANDA NO. 74-910

Dear Mr. Sporn:

Pursuant to Section 505(j)(2)(A)(vii) of the Federal Food, Drug and Cosmetic Act, Mylan certifies that in its opinion and to the best of its knowledge, U.S. Patent 4,721,619 is invalid, unenforceable or will not be infringed by the manufacture, use, sale, offer for sale, or importation of Diltiazem Hydrochloride Extended-Release Capsules USP 60mg, 90mg, and 120mg, for which this application is submitted.

Mylan further certifies that according to the exclusivity information published by the FDA in that document entitled "Approved Drug Products with Therapeutic Equivalence" 16th Edition and the fifth Supplement thereto, the referenced product is not covered by any exclusivity.

Mylan will market its Diltiazem Hydrochloride Extended-Release capsules upon approval of this application and resolution of the validity, enforcement, or infringement of patent number 4,721,619.

Sincerely,

Dawn J. Beto, Esq.
Senior Counsel

DJB/dc

Department—Fax Numbers		Information Systems	(304) 598-5404	Purchasing	(304) 598-5401
Accounting	(304) 598-5403	Label Control	(800) 848-0463	Quality Control	(304) 598-5407
Administration	(304) 599-7284	Legal Services	(304) 598-5408	Research & Development	(304) 598-5409
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		

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

September 24, 1996

NEW CORRESP
NC

Offices 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: DILTIAZEM HYDROCHLORIDE EXTENDED RELEASE CAPSULES USP, 60MG, 90MG AND 120MG
ANDA NO. 74-910

Dear Mr. Sporn:

Pursuant to 21 CFR 314.95(e), Mylan hereby amends the above referenced application with documentation of receipt of the notice required by 21 CFR 314.95(a). I have enclosed documentation of receipt by the owner of the patent, and the holder of the application for the listed drug claimed by said patent. Proof of delivery from Federal Express evidences receipt by Elan Corporation on August 15, 1996, and Certified Mail, Return Receipt evidences receipt by Hoechst Marion Roussel on August 16, 1996.

Sincerely,

Dawn J. Beto, Esq.
Senior Counsel

RECEIVED
SEP 26 1996
CENTER FOR

DJB/dc

Enclosures

Department—Fax Numbers
Accounting (304) 598-5403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 598-5404
Label Control (800) 848-0463
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Research & Development (304) 598-5409
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

NEW CORRESP

November 11, 1996

BIOAVAILABILITY
NC/RIO

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

BIOEQUIVALENCE DATA ENCLOSED

RE: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES, USP
60MG, 90MG, and 120MG
ANDA 74-910
RESPONSE TO AGENCY LETTER DATED OCTOBER 31, 1996

Dear Mr. Sporn:

Reference is made to the ANDA identified above for Diltiazem Hydrochloride Extended-release Capsules, USP 60 mg 90 mg and 120 mg and to the Agency letter dated October 31, 1996. In response to the referenced comment letter, Mylan's reply is as follows:

REGARDING BIOEQUIVALENCY ISSUES:

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

MYLAN RESPONSE: Mylan acknowledges that the Division of Bioequivalence has completed its review of the *in vivo* bioequivalence studies submitted in support of the above referenced ANDA and has no further questions at this time.

FDA COMMENT 2. The following interim dissolution testing will need to be incorporated into your stability and quality control programs:

The dissolution testing should be conducted in 900 mL of water at 37°C using USP 23 apparatus 2 (Paddle) at 100 rpm. The test products should meet the following specifications:

4 hours	%
8 hours	%
12 hours	%
24 hours	NLT %

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
Label Control (800) 848-0463
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 RESPONSE: The dissolution testing requested above has been incorporated into Mylan's stability and quality control programs for Diltiazem Hydrochloride Extended-release Capsules, USP 60mg, 90mg and 120mg. This testing is identical to that currently proposed by Mylan and submitted to the Agency in Mylan's Diltiazem Hydrochloride Extended-release Capsules USP, 60mg, 90mg, and 120 mg ANDA on June 12, 1996.

Should you require additional information or have any questions regarding this amendment, please contact the undersigned at (304) 599-2595, ext. 6600/fax (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

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

JAN 15 1997

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

MINOR AMENDMENT

RE: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES USP (TWICE-A-DAY-DOSAGE), 60 MG, 90 MG, AND 120 MG
ANDA 74-910
AGENCY LETTER DATED DECEMBER 27, 1996

Dear Mr. Sporn:

In response to the above referenced letter, we wish to amend the referenced application as follows:

REGARDING CHEMISTRY ISSUES:

Department Fax Numbers

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

GENERIC DRUGS

Redacted 2

pages of trade

secret and/or

confidential

commercial

information

Chem issues

REGARDING LABELING ISSUES:

MYLAN RESPONSE: Attachment M contains twelve (12) copies of the following final printed bottle labels and prescribing information for Diltiazem Hydrochloride Extended-release Capsules, USP (Twice-a-Day Dosage), 60 mg, 90 mg, and 120 mg:

BOTTLE LABELS:

60 mg: Code RM6060A1 - Bottles of 100 Capsules

90 mg: Code RM6090A1 - Bottles of 100 Capsules

120 mg: Code RM6120A1 - Bottles of 100 Capsules

PACKAGE OUTSERT:

Code DILER:R1 - Revised January 1997

The enclosed labeling incorporates the revisions requested in the Agency's letter of December 27, 1996. A copy of the December 27 letter is provided in Attachment J for the convenience of the reviewer.

In order to facilitate the review of this labeling, Attachment K contains a side-by-side comparison of the final printed bottle labeling to the draft bottle labeling that was previously submitted. Attachment L contains a side-by-side comparison of the final printed prescribing information to the draft information that was previously submitted. It is noted that further revisions to this labeling may be requested prior to the approval of this application.

Pursuant to 21 CFR 314.94(d)(5), we certify that a true copy of this minor amendment as submitted to the Office of Generic Drugs has been forwarded to the FDA's Baltimore District Office.

Any questions or concerns regarding this minor amendment should be addressed to the attention of the undersigned at telephone number (304) 599-2595, ext. 6600 or via facsimile at (304) 285-6407.

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

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

NEW CORRESP

NC

April 1, 1997

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

ATTENTION: MR. PETER RICKMAN

CORRESPONDENCE

RE: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES, USP
60MG, 90MG, AND 120MG
ANDA #74-910
RESPONSE TO AGENCY TELEPHONE CALL OF APRIL 1, 1997

Dear Mr. Rickman:

Attached, as requested, is a letter regarding our "Paragraph IV" Certification pertaining to the above ANDA which states that Mylan was not sued during the 45-day period following notification of receipt of the "Paragraph IV" Certification by the patent/application holder(s).

Sincerely,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

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APR 0 3 1997

Department Fax Number
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources (304) 598-5406
Information Systems (304) 285-6404
Label Control (800) 848-0463
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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

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

November 12, 1996

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: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES USP 60 MG, 90 MG AND 120 MG
ANDA NO. 74-910

Dear Mr. Sporn:

On August 13, 1996, Mylan amended its application for the above-referenced products, with a "Paragraph IV" certification. Pursuant to Section 505(j)(2)(B)(I) of the Federal Food, Drug and Cosmetic Act and 21 CFR 314.95(d), Mylan provided notice to Elan Corporation, as owner of U.S. Patent 4,721,619, and also to Hoechst Marion Roussel as the application holder for the listed drug claimed by said patent. Said notice complied with requirements set forth in 21 CFR 314.95(c), with respect to the content of the notice, and was received by Elan Corporation on August 15, 1996, and Hoechst Marion Roussel on August 16, 1996. On September 24, 1996, Mylan provided FDA with documentation of receipt of the notice by Elan Corporation and Hoechst Marion Roussel, as required by 21 CFR 314.95. The 45 day period, as provided by Section 505(c)(3)(C) of the FFDCA, in which Elan Corporation or Hoechst Marion Roussel could sue Mylan expired on September 29, 1996 and September 30, 1996, respectively. Mylan has received no notice of the institution of a lawsuit by either of the afore-mentioned entities. Mylan therefore believes that the Agency is clear to issue a final approval for the above-referenced application upon satisfactory completion of the regulatory review process.

Sincerely,

Dawn J. Beto, Esq.
Senior Counsel

DJB/pp

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

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

April 30, 1997

NEW CORRESP

VIA FACSIMILE

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: DILTIAZEM HCl EXTENDED-RELEASE CAPSULES, USP
60 mg, 90 mg & 120 mg
ANDA 74-910

Dear Mr. Sporn:

Pursuant to our conversation on this date with Mr. Jerry Phillips, Mylan commits to delete the statement

> *"Diltiazem Hydrochloride Extended-release Capsules, USP which exhibit different pharmacokinetics are also marketed. Please confirm you are dispensing the prescribed formulation."*

from both the container label and the package insert prior to marketing this product.

Sincerely,

John O'Donnell

John P. O'Donnell, Ph.D.
Executive Vice President

RECEIVED
MAY 0 1
GENERIC DRUGS

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
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Human Resources	(304) 598-5406	Medical Unit	(304) 598-5445		

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG FOR HUMAN USE OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314)

Form Approved: OMB No. 0910-0001. Expiration Date: December 31, 1999. See OMB Statement on Page 3.

FOR FDA USE ONLY

DATE RECEIVED	DATE FILED
DIVISION ASSIGNED	NDA/ANDA NO. ASS.

NOTE: No application may be filed unless a completed application form has been received *(21 CFR Part 314)*.

NAME OF APPLICANT
MYLAN PHARMACEUTICALS INC.

DATE OF SUBMISSION
April 30, 1997

TELEPHONE NO. *(Include Area Code)*
(304) 599-2595

ADDRESS *(Number, Street, City, State and ZIP Code)*
781 Chestnut Ridge Road
P.O. Box 4310
Morgantown, WV 26504-4310

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER *(If previously issued)*
74-910

DRUG PRODUCT

ESTABLISHED NAME *(e.g., USP/USAN)*
Diltiazem Hydrochloride
Extended-Release Capsules, USP

PROPRIETARY NAME *(If any)*
NA

CODE NAME *(If any)*
NA

CHEMICAL NAME
1,5-Benzothiazepin-4(5H)-one, 3-(acetyloxy)-5-[2-(dimethylamino) ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride, (+)-cis-

DOSAGE FORM
Capsule

ROUTE OF ADMINISTRATION
Oral

STRENGTHS (S)
60 mg, 90 mg
120 mg

PROPOSED INDICATIONS FOR USE
Treatment of Hypertension

LIST NUMBERS OF ALL INVESTIGATIONAL NEW DRUG APPLICATIONS *(21 CFR Part 312)*, NEW DRUG OR ANTIBIOTIC APPLICATIONS *(21 CFR Part 314)*, AND DRUG MASTER FILES *(21 CFR 314.420)* REFERRED TO IN THIS APPLICATION:

DMF
DMF
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DMF

INFORMATION ON APPLICATION

TYPE OF APPLICATION *(Check one)*

☐ THIS SUBMISSION IS A FULL APPLICATION *(21 CFR 314.50)*
☒ THIS SUBMISSION IS AN ABBREVIATED APPLICATION (ANDA) *(21 CFR 314.55)*

IF AN ANDA, IDENTIFY THE APPROVED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

NAME OF DRUG
Cardizem® SR

HOLDER OF APPROVED APPLICATION
Marion Merrell Dow Inc. (Hoechst Marion Roussel Inc.)

TYPE SUBMISSION *(Check one)*

☐ PRESUBMISSION
☐ ORIGINAL APPLICATION
☐ AN AMENDMENT TO A PENDING APPLICATION
☐ RESUBMISSION
☐ SUPPLEMENTAL APPLICATION

SPECIFIC REGULATION(S) TO SUPPORT CHANGE OF APPLICATION *(e.g., Part 314.70(b)(2)(v))*: _____

PROPOSED MARKETING STATUS *(Check one)*

☐ APPLICATION FOR A PRESCRIPTION DRUG PRODUCT *(Rx)*
☐ APPLICATION FOR AN OVER-THE-COUNTER PRODUCT *(OTC)*

CONTENTS OF APPLICATION

This application contains the following items: *(Check all that apply)*

	1. Index
	2. Summary (21 CFR 314.50) (c))
	3. Chemistry, manufacturing, and control section (21 CFR 314.50 (d) (1))
	4. a. Samples (21 CFR 314.50 (e) (1)) (Submit only upon FDA's request)
	b. Methods Validation Package (21 CFR 314.50 (e) (2) (i))
	c. Labeling (21 CFR 314.50 (e) (2) (ii))
	i. draft labeling *(4 copies)*
	ii. final printed labeling (12 copies)
	5. Nonclinical pharmacology and toxicology section (21 CFR 314.50 (d) (2))
	6. Human pharmacokinetics and bioavailability section (21 CFR 314.50 (d) (3))
	7. Microbiology section (21 CFR 314.50 (d) (4))
	8. Clinical data section (21 CFR 314.50 (d) (5))
	9. Safety update report (21 CFR 314.50 (d) (5) (vi) (b))
	10. Statistical section (21 CFR 314.50 (d) (6))
	11. Case report tabulations (21 CFR 314.50 (f) (1))
	12. Case reports forms (21 CFR 314.50 (f) (1))
	13. Patent information on any patent which claims the drug (21 U.S.C. 355 (b) or (c))
	14. A patent certification with respect to any patent which claims the drug (21 U.S.C 355 (b) (2) or (j) (2) (A))
X	15. OTHER *(Specify)* Response to Agency phone call of this date

I agree to update this application with new safety information about the drug that may reasonably affect the statements of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit these safety update reports as follows: (1) 4 months after the initial submission, (2) following receipt of an approvable letter and (3) at other times as requested by FDA. If this application is approved, I agree to comply with all laws and regulations that apply to approved applications, including the following:

1. Good manufacturing practice regulations in 21 CFR 210 and 211.
2. Labeling regulations in 21 CFR 201.
3. In the case of a prescription drug product, prescription drug advertising regulations in 21 CFR 202.
4. Regulations on making changes in application in 21 CFR 314.70, 314.71, and 314.72.
5. Regulations on reports in 21 CFR 314.80 and 314.81.
6. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

NAME OF RESPONSIBLE OFFICIAL OR AGENT	SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	DATE
John O'Donnell		4/30/97

ADDRESS *(Street, City, State, ZIP Code)*	TELEPHONE NO. *(Include Area Code)*
781 Chestnut Ridge Road, P.O. Box 4310 Morgantown, WV 26504-4310	(304) 599-2595

WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

MYLAN PHARMACEUTICALS INC

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

JUN 12 1996

RECEIVED

JUN 13 1996

GENERIC DRUGS

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

BIOEQUIVALENCE DATA ENCLOSED
ELECTRONIC DATA ENCLOSED

RE: DILTIAZEM HYDROCHLORIDE EXTENDED-RELEASE CAPSULES, USP
60 MG, 90 MG AND 120 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: Diltiazem Hydrochloride Extended-release Capsules
This application consists of a total of 27 volumes.
Archival Copy - 12 volumes.
Review Copy - 13 volumes.
Technical Section For Chemistry - 3 volumes.
Technical Section For Pharmacokinetics - 10 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 diskette for the bioequivalence studies.

This application provides for the manufacture of three strengths of Diltiazem Hydrochloride Extended-release Capsules containing 60 mg, 90 mg or 120 mg of diltiazem hydrochloride. 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 field copy, which is a true copy of the technical sections of this application , has been submitted to the Baltimore District Office.

For more detailed information regarding the organization of this ANDA, please refer to the Reader's Guide and Master Table of Contents following this letter.

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,

Frank R. Sisto
Executive Director
Regulatory Affairs

FRS/tlm

enclosures

Department	
Accounting	(304) 598-5403
Administration	(304) 599-7284
Business Development	(304) 599-7284
Human Resources	(304) 598-5406
Information Systems	(304) 598-5404
Label Control	(800) 848-0463
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) 598-5409
Sales & Marketing	(304) 598-3232