CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-424

CORRESPONDENCE

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

July 27, 2001

ORIG AMENDMENT
N/FA.

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

TELEPHONE AMENDMENT
(CMC INFORMATION ENCLOSED)

RE: SPIRONOLACTONE TABLETS USP, 25MG, 50MG AND 100MG
ANDA 40-424
RESPONSE TO AGENCY TELEPHONE REQUEST OF JULY 6, 2001

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application (ANDA) identified above, which is currently under review, and to the Agency's telephone request of July 6, 2001. During the July 6th telephone call with Dr. Albert Mueller and Dr. Andre Ra, the Agency expressed concern about the perceived consistent loss of value on assay from release through stability for all bottle sizes and strengths of Spironolactone Tablets, USP. In order to assess this trend prior to approval, it was requested that Mylan test room temperature stability samples at 15 months, using Mylan's proposed ; assay method.

As requested by the Agency on July 6, 2001, Mylan hereby provides room temperature stability through the 15 month time point for Spironolactone Tablets USP, 25mg, 50mg and 100mg (Attachment A). Both the USP assay method and Mylan's proposed assay method are provided on the stability data tables. Mylan believes that this stability data, as well as previously submitted accelerated, intermediate and room temperature stability data continue to justify a 24 month expiration date. All strengths of Spironolactone Tablets, USP are stable and all results are within normal levels of analytical variability.

We trust that the information provided in this amendment will be considered sufficient to support approval of this application with the originally requested expiration dating period of 24 months.

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,

Vincent Mancinelli II for

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn

Enclosures

cc: Tim Ames, Project Manager, OGD/CDER/FDA (via facsimile)

G:\PROJECT\ANDA\SPIRONOLACTONE\New-Formulation\AGENCY-TELEPHONE-REQUEST-070601.doc

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		

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

June 27, 2001

ORIG AMENDMENT
AF

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

LABELING AMENDMENT

RE: SPIRONOLACTONE TABLETS USP, 25 mg, 50 mg and 100 mg
ANDA 40-424
RESPONSE TO AGENCY CORRESPONDENCE DATED MAY 31, 2001

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application for spironolactone, identified above, which is currently under review. Reference is also made to the Agency's correspondence dated May 31, 2001, which provided the Agency's comments on Mylan's proposed outsert and bottle labels. A copy of the Agency's May 31st correspondence is provided in Attachment 1. Mylan revised the labeling pursuant to the Agency's suggestions.

Accordingly, we wish to amend the above-referenced application with the final printed outsert and corresponding bottle labels. Enclosed in Attachment 4 are twelve (12) copies of the outsert Code SP:R16, Revised June 2001and twelve (12) copies of the final printed bottle labels as follows:

25 mg		
Code	RM2146A7	Bottles of 100 Tablets
Code	RM2146B5	Bottles of 500 Tablets
50 mg		
Code	RM0243A	Bottles of 100 Tablets
Code	RM0243B	Bottles of 500 Tablets
100 mg		
Code	RM0437A	Bottles of 100 Tablets
Code	RM0437B	Bottles of 500 Tablets

The labeling revisions are described in the annotations provided in the side-by-side comparison of the revised labeling to Mylan's previously-submitted labeling. The side-by-side comparison of Mylan's final printed bottle labels to the previously-submitted draft bottle labels is provided in Attachment 2. The side-by-side comparison of Mylan's revised final printed outsert to the previously-submitted draft outsert (code SP:R16X) is provided in Attachment 3.

G:\PROJECT\ANDA\SPIRONOLACTONE\AGENCY FAX DATED 053101.doc

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

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

dmy/enclosures

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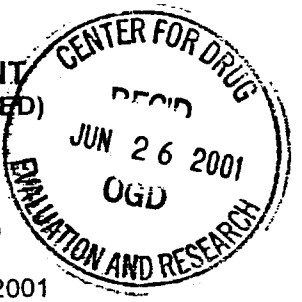
MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

June 25, 2001

ORIG AMENDMENT
N/FA

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

TELEPHONE AMENDMENT
(CMC INFORMATION ENCLOSED)



RE: SPIRONOLACTONE TABLETS USP, 25MG, 50MG AND 100MG
ANDA 40-424
RESPONSE TO AGENCY CORRESPONDENCE OF JUNE 18, 2001

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the comments pertaining to this application which were provided to Mylan by facsimile in a correspondence dated June 18, 2001 (refer to Attachment B). In response to the comments in the June 18, 2001 correspondence, Mylan wishes to amend its ANDA as follows:

FDA COMMENT 1: Your room temperature stability data (3, 6, 9, 12 months) indicates a significant

MYLAN RESPONSE:

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		

FDA COMMENT 2:

MYLAN RESPONSE:

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We trust that the information provided in this amendment will be considered sufficient to support approval of this application with the originally requested expiration dating period of 24 months.

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/dn

Enclosures

G:\PROJECT\ANDA\SPIRONOLACTONE\New-Formulation\AGENCY-LETTER-DATED-061801.doc

FA noted
To CMC Reviewer for review.
5/16/01

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

May 10, 2001

ORIG AMENDMENT
N/FA

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: SPIRONOLACTONE TABLETS USP, 25MG, 50MG AND 100MG
ANDA 40-424
RESPONSE TO AGENCY CORRESPONDENCE OF APRIL 12, 2001

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application identified above, which is currently under review, and to the comments pertaining to this application which were provided to Mylan by facsimile in a correspondence dated April 12, 2001 (refer to Attachment P). In response to the comments in the April 12, 2001 correspondence, Mylan wishes to amend its ANDA as follows:

A. CHEMISTRY DEFICIENCIES

1. Regarding the active ingredient, Spironolactone, USP, we have the following comments:

FDA COMMENT 1a:

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MYLAN RESPONSE:

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has

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FDA COMMENT 1b:

s
ts

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times in your COA.

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		

Page(s) 5

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

5/10/01

In the Agency's April 12, 2001 correspondence (included in Attachment P), comments from the Division of Bioequivalence were also provided. These comments listed the dissolution testing requirements for Spironolactone Tablets USP, 25mg, 50mg and 100mg to be incorporated into Mylan's stability and quality control programs. A separate amendment, acknowledging the comments from the Division of Bioequivalence will be forwarded simultaneously with this CMC amendment.

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,

Vincent Mancinelli II 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

NAI, "Bio Submission"

December 13, 2000

40424

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

NEW CORRESP
NK/BIO

RE: SPIRONOLACTONE TABLETS, USP
25 mg, 50 mg and 100 mg

BIOEQUIVALENCE ELECTRONIC SUBMISSION ESD

Dear Mr. Buehler:

Reference is made to the Abbreviated New Drug Application (ANDA) for the referenced product that was submitted to the Agency on November 13, 2000. Please find enclosed a diskette providing the electronic submission, ESD, for the bioequivalence studies (100 mg fasting study SPIR-0013 and 100 mg post-prandial study SPIR-0014) that were submitted in the ANDA. A copy of Mylan's declaration that the data contained on the electronic bioequivalence diskette is identical to the paper submission except as noted in the companion document is presented in Attachment 1.

Should you have any questions or require additional information, please contact the undersigned at telephone number (304) 599-2595, extension 6600 and/or facsimile number (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

/Enclosures

CENTER FOR DRUG
RECD
DEC 15 2000
OGD
EVALUATION AND RESEARCH

Department—Fax Numbers
Accounting (304) 285-6403
Administration (304) 599-7284
Business Development (304) 599-7284
Human Resources G:\PROJECT\ANDA\[illegible]\SPIRONOLACTONE\New-Form\Mod\NEW.doc
Information Systems (304) 285-6404
Label Control (800) 848-0463
Legal Services (304) 598-5408
Maintenance & Engineering (304) 598-5411
(304) 598-5445
Purchasing (304) 598-5401
Quality Control (304) 598-5407
Research & Development (304) 285-6409
Sales & Marketing (304) 598-3232

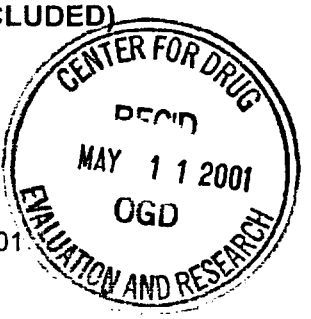
MYLAN PHARMACEUTICALS INC
781 Chestnut Ridge Road • P. O. Box 4310 • Morgantown, West Virginia 26504-4310 U.S.A. • (304) 599-2595

May 10, 2001

NEW CORRESP
NC/BIO

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

BIOEQUIVALENCE AMENDMENT
(CMC INFORMATION INCLUDED)



RE: SPIRONOLACTONE TABLETS USP, 25MG, 50MG AND 100MG
ANDA 40-424
RESPONSE TO AGENCY CORRESPONDENCE DATED APRIL 12, 2001

Dear Mr. Buehler:

Reference is made to the ANDA identified above, which is currently under review, and to the comments from the Division of Bioequivalence pertaining to this application which were included in the Agency's facsimile correspondence that was forwarded to Mylan on April 12, 2001. In response to the April 12th correspondence from the Division of Bioequivalence, Mylan wishes to amend the application as follows:

1. REGARDING BIOEQUIVALENCE ISSUES:

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

We acknowledge that the dissolution testing has been incorporated into your stability and quality control programs as specified in USP 24.

Consistent with the CDER Guidance for Industry "Bioavailability and Bioequivalence Studies for Orally Administered Drug Products – General Considerations", posted 10/27/00, the Division of Bioequivalence now requests that spironolactone be assayed in plasma and analyzed using a confidence interval approach. This criteria will be applied to any bioequivalence studies of spironolactone initiated after the guidance was issued. Since spironolactone can be reliably measured in plasma, canrenone need not be assayed.

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.

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		

MYLAN RESPONSE: As acknowledged by the Division of Bioequivalence, the dissolution testing requirements for Spironolactone Tablets, 25mg, 50mg and 100mg have already been incorporated into Mylan's stability and quality control programs. No further action is, therefore, considered necessary.

Mylan acknowledges that consistent with the CDER Guidance for Industry – "Bioavailability and Bioequivalence Studies for Orally Administered Drug Products – General Considerations," posted 10/27/00, the Division of Bioequivalence now requests that Spironolactone be assayed in plasma and analyzed using a confidence interval approach. It is Mylan's understanding that this criteria will be applied to any bioequivalence studies of Spironolactone initiated after the guidance was issued and that since Spironolactone can be reliably measured in plasma, canrenone need not be assayed. It should be noted that Mylan initiated its fasting and post-prandial bioequivalence studies on April 14, 2000 and April 18, 2000, respectively; therefore, the studies were completed prior to the issuance of the guidance.

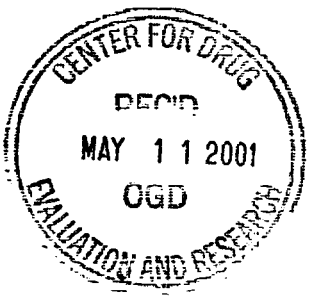
It is acknowledged and understood that the bioequivalency comments expressed in the correspondence dated April 12, 2001 are preliminary and may be revised after review of the entire application. It is also understood that the reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

For your reference, a copy of the April 12, 2001 Agency correspondence is provided in Attachment A. Responses to the chemistry comments contained in the April 12th correspondence will be forwarded simultaneously in a separate amendment to this application.

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

ANDA 40-424

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

DEC 19 2000

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 December 15, 2000.

NAME OF DRUG: Spironolactone Tablets USP, 25 mg, 50 mg and 100 mg

DATE OF APPLICATION: November 13, 2000

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 14, 2000

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) 827-5848

Sincerely yours,

Gregory S. Davis for

Wm Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-424 APPLICANT: Mylan Pharmaceuticals Inc.

DRUG PRODUCT: Spironolactone Tablets USP, 25 mg, 50 mg and 100 mg

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

We acknowledge that the dissolution testing has been incorporated into your stability and quality control programs as specified in USP 24.

Consistent with the CDER Guidance for Industry "Bioavailability and Bioequivalence Studies for Orally Administered Drug Products - General Considerations", posted 10/27/00, the Division of Bioequivalence now requests that spironolactone be assayed in plasma and analyzed using a confidence interval approach. This criteria will be applied to any bioequivalence studies of spironolactone initiated after the guidance was issued. Since spironolactone can be reliably measured in plasma, canrenone need not be assayed.

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,

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

APR 12 2001

38. Chemistry Comments to be Provided to the Applicant:

ANDA: 40-424 APPLICANT: Mylan Pharmaceuticals Inc

DRUG PRODUCT: Spironolactone Tablets USP, 25 mg, 50 mg and 100 mg

The deficiencies presented below represent FAX deficiencies.

A. Chemistry Deficiencies

1. Regarding the active ingredient, Spironolactone USP, we have following comments:

   a. In regard to your proposed limit for the of spironolactone, we suggest that you either demonstrate that this impurity is present in the innovator's product at levels comparable to your proposed limits , or that the limits be tightened based upon observed values.

   b. In regard to your limits for other individual impurities , we suggest that you either demonstrate that each of these individual unknown impurities is present in the innovator's product at these levels, or that you tighten your limits based upon observed values. Furthermore, we do acknowledge that a few of your individual unknown impurities will require limits that exceed We suggest that those impurities be specifically identified by their relative retention times in your COA.

   c. We note that Spironolactone USP does not include any testing for residual solvents. We suggest that you contact your bulk drug substance supplier and establish suitable specifications for residual solvents.

   d. We note that Spironolactone USP does not include any testing for "Residue on Ignition" or "Heavy Metals". Please establish suitable specifications which assure drug product safety.

   e. We suggest that you include a specification for drug substance polymorph (identification), preferably by Otherwise, please demonstrate that the polymorphic forms of the drug substance do not have significantly different properties.

2. Please have your supplier cite applicable CFR references in regard to all the ingredients used in the peppermint flavor formulation. If possible, please provide a list of approved drug products, which utilize the same peppermint flavor in their drug product formulation.

3. Please provide suitable container permeation data per USP <671>. Please note that if the container closure system has an inner seal, it should be removed prior to testing. Please refer to the *FDA Guidance for Industry on Container Closure Systems for Packaging Human Drugs and Biologics (III.G)*.

4. Regarding the controls of your finished dosage form and your stability test results, we have the following comments:

a.

d

b.

c.

d.

your drug substance.

e.

f.

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

1. Labeling review is pending. You will be notified on the status of the labeling review under a separate cover.

2. Please provide any additional stability data accrued to date.

3. Your analytical methodology is not identical to the US Pharmacopeial method for the final drug product. Please be advised that the USP methods are the regulatory methods and will prevail in the event of any 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: 40-424 APPLICANT: Mylan Pharmaceuticals Inc.

DRUG PRODUCT: Spironolactone Tablets USP, 25 mg, 50 mg and 100 mg

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

We acknowledge that the dissolution testing has been incorporated into your stability and quality control programs as specified in USP 24.

Consistent with the CDER Guidance for Industry "Bioavailability and Bioequivalence Studies for Orally Administered Drug Products - General Considerations", posted 10/27/00, the Division of Bioequivalence now requests that spironolactone be assayed in plasma and analyzed using a confidence interval approach. This criteria will be applied to any bioequivalence studies of spironolactone initiated after the guidance was issued. Since spironolactone can be reliably measured in plasma, canrenone need not be assayed.

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,

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

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

505(b)(2) OK
19-DEC-2000

November 13, 2000

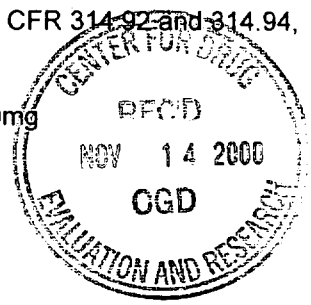
ELECTRONIC DATA ENCLOSED
BIOEQUIVALENCE DATA ENCLOSED

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

RE: SPIRONOLACTONE TABLETS USP, 25MG, 50MG and 100MG

Dear Mr. Buehler:

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: Spironolactone Tablets USP, 25mg, 50mg and 100mg
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 set of data diskettes for the bioequivalence studies conducted in support of this application. In addition, the diskettes providing the Bioequivalence Electronic Submission ESD (BA/BE) EVA will be forwarded to the Agency within the 30 day grace period.

This application provides for the manufacture of Spironolactone Tablets USP, 25mg, 50mg and 100mg. Mylan Pharmaceuticals Inc., 781 Chestnut Ridge Road, Morgantown, WV 26505-2730, performs all operations in the manufacture, packaging, and labeling of the drug product.

It should be noted that Mylan Pharmaceuticals Inc. currently manufactures and markets Spironolactone Tablets USP, 25mg under ANDA 87-086. This new application, supported by both fasting and fed *in-vivo* bioequivalence studies, is totally independent of ANDA 87-086 and provides for the manufacture and marketing of 25mg, 50mg and 100mg Spironolactone Tablets, USP. The formulation and manufacturing process for the Spironolactone Tablets contained in this application have been revised to enhance manufacturing efficiency.

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 Abbreviated New Drug Application has been organized according to the Agency's February 1999 Guidance for Industry - 'Organization of an ANDA'. Pursuant to this guidance, Mylan commits to resolve any issues identified in the methods validation process after approval.

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. Telephone and facsimile inquiries may also be directed to the undersigned at telephone number (304) 599-2595, extension 6600 and/or facsimile number (304) 285-6407.

Sincerely,

Frank R. Sisto
Vice President
Regulatory Affairs

FRS/dn