CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756/S-006 and S-009

Name: Primaxin ADD-Vantage
(Imipenem-Cilastatin Sodium for Injection)

Sponsor: Merck Sharp & Dohme Research Laboratories

Approval Date: September 9, 1991

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-006 and S-009

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Tentative Approval Letter	
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Statistical Review	
Microbiology Review	
Administrative Documents	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-006 and S-009

APPROVAL LETTER

AADA 62-756/S-006,009

Merck Sharp & Dohme Research Laboratories
Attn: Ronald A. Salerno, Ph.D.
Sumneytown Pike
West Point, PA 19486

SEP 9 1991

Dear Sir:

Reference is made to your supplemental antibiotic drug applications submitted pursuant to Section 314.70 of the Regulations, dated May 29, 1990 and April 17, 1991 , regarding your abbreviated antibiotic application for Primaxin® ADD-Vantage® (Imipenem-Cilastatin Sodium, MSD).

Reference is also made to your communications of June 21, July 31, and August 21, 1991 amending these supplemental applications.

The supplemental applications provide for manufacturing process changes which permit use of a preferred bulk drug synthesis route which eliminates ———————— from the manufacturing process.

We have completed the review of these supplemental applications and they are approved. Our letter of January 8, 1987 detailed the conditions relating to the approval of this abbreviated application.

The material submitted is being retained as part of your application.

Sincerely yours,

Robert A. Jerussi 9/7/91

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

cc: AADA # 62-756/S-009
DUP/Division File
HFD-600/RF
HFC-130/JAllen
HFD-520/DeCamp
HFD-520/Roy
HFD-520/Lumpkin
HFD-635/RF
HFD-635/JHarrison/EDuffy/ ~~2/20/91~~ 9/4/91
HFD-635/JHannan JHannan 9/5/91
R/D initialed by JHarrison
mw/9/4/91/62-756S.009
F/T by mw/9/4/91
SUPPLEMENT APPROVAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-006 and S-009

CHEMISTRY REVIEW

AADA 62-756/S-006,009

NAME AND ADDRESS OF APPLICANT:

Merck Sharp & Dohme Research Laboratories
Attn: Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Liason
Sumneytown Pike
West Point, PA 19486

Contact:
Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Liason
(215) 834-2958
or
Kenneth R. Brown, M.D.
(215) 834-2552

PURPOSE OF AMENDMENT/SUPPLEMENT

The supplemental applications provide for manufacturing process changes which permit use of a preferred bulk drug synthesis route which eliminates ———————— from the manufacturing process.

DATE(S) OF SUBMISSION(S)

5/29/90 - S-006 submitted
4/17/91 - S-009 submitted
4/26/91 - request for expedited review accepted
5/7/91 - telecon EPD/FDA to KBrown/MSD
5/13/91 - telecon EPD/FDA to RSalerno/MSD
6/21/91 - amendment to S-009
7/24/91 - telecon EPD/FDA to RSalerno/MSD
7/31/91 - amendment to S-006,009
8/13/91 - telecon EPD/FDA to RSalerno/MSD
8/21/91 - amendment to S-006,009

PHARMACOLOGICAL CATEGORY
Antibiotic

TRADE NAME
Primaxin® ADD-Vantage®

NONPROPRIETARY NAME
Imipenem-Cilastatin Sodium

DOSAGE FORM
Powder for reconstitution

POTENCY
250, 500 mg

RX OR OTC
R

SAMPLES	RELATED IND/NDA/DMF
N/A	50-587/S-028 ——— Primaxin® IV
	50-630/S-006,009 Primaxin® IM

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION
N/A
[Manufacturing done at Merck's Danville PA mfg. facility]

COMPONENTS

COMPOSITION

MANUFACTURING

[redacted]

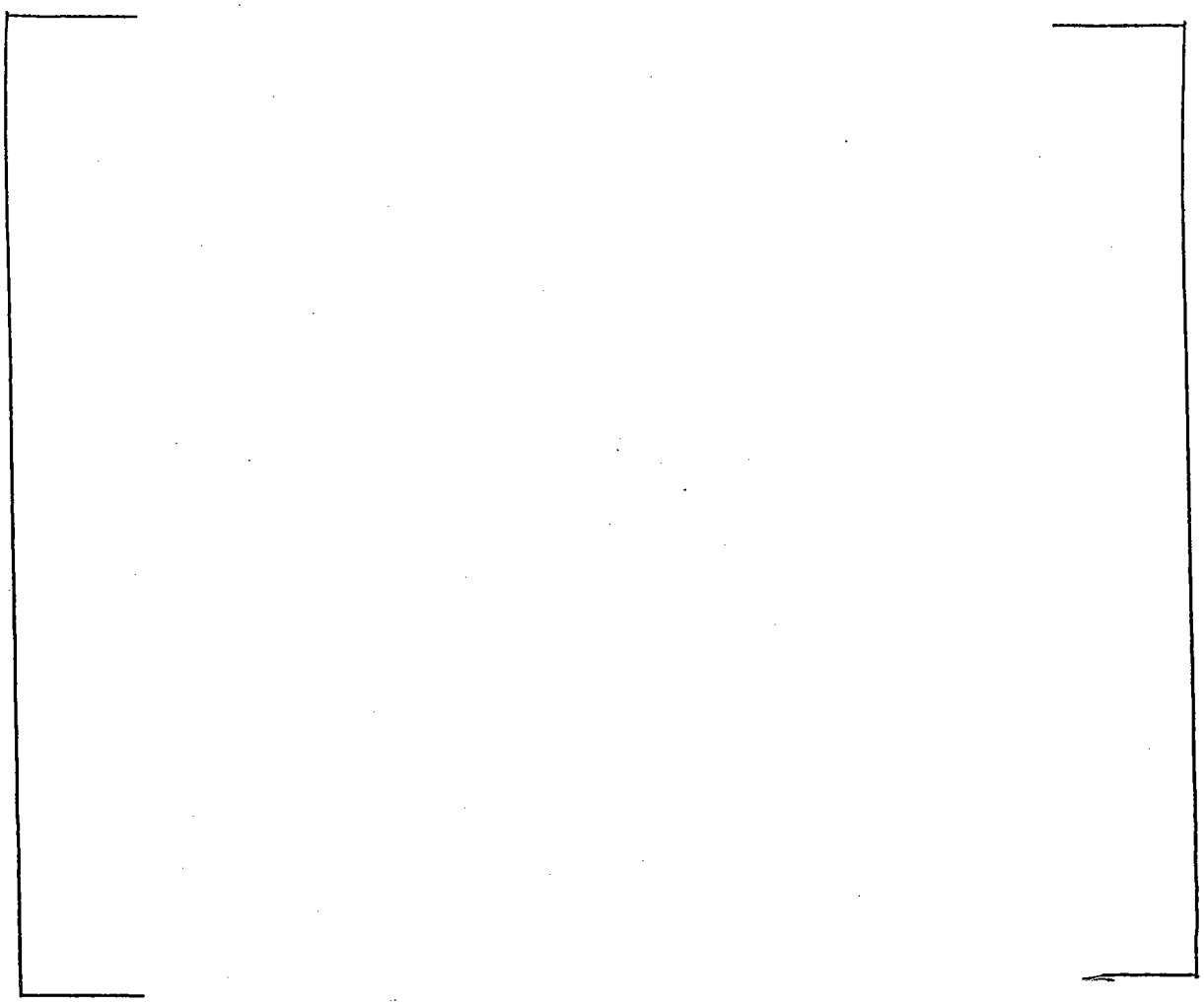
Redacted 2 page(s)

of trade secret and/or

confidential commercial

information from

CHEMISTRY REVIEW #1



PACKAGING
N/A

STABILITY
N/A

REMARKS AND CONCLUSION

Process changes to remove ——— from the process are proposed in order to meet a commitment by Merck to acheive a ——— ———. The process described is identical to the processes in 50-587 and 50-630, and a coordinated response has been discussed.

Narrative descriptions of the proposed synthesis ——— on a production scale are provided for Imipenem, but not for

Cilastatin Sodium. The proposed synthesis process for Cilastatin Sodium is described only on a laboratory scale.

The proposed process appears to be acceptable. Controls for ——————— will be established if detectible levels are found in initial production batches. In consultation with Dr. Suva Roy/HFD-520 to coordinate responses, the firm has been requested to provide a commitment to provide ——————— ——————— data from production batches, and if found, specifications and tests will be established. The firm has provided validated methods for ——————— determination, and commits to provide a descriptions of the production scale process.

APPROVAL RECOMMENDED

RECALLS	Reviewer	Date Completed
	Eric P. Duffy	

cc: AADA # 62-956/S-009
Review Chemist's name: Eric P. Duffy EDuffy/9-4-91
Supervisor's name: John D. Harrison

9/4/91

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-006 and S-009

ADMINISTRATIVE DOCUMENTS

EXPEDITED REVIEW REQUESTED

ANDA: N62-756/S-009 **FIRM:** MSD **DRUG:** PRIMAXIN I.V. ADD-VANTAGE

DATE: 4/25/91 **DATE OF SUPPLEMENT:** 4/17/91

The Division of Generic Drugs, Policy and Procedure Guide 18-90 lists the following criteria for granting an Expedited Review Request.

1. Supplements regarding to pending legal/regulatory action or need by the government's drug purchase program will be considered upon request from the appropriate FDA office.
2. Supplements regarding Federal or State legal or regulatory actions, including mandated formulation changes or labeling changes.
3. Supplements pertaining to an event that was outside the control of the applicant and could not have been reasonably and adequately planned for (as: natural disater, fire, abrupt discontinuation of supply of active ingredient, packaging material, or container closure system) and that prevents the marketing of one or more products.
4. Supplements for relocation of a facility will be considered if it is undertaken for the purpose of maintaining or significantly enhancing assurance of high manufacturing standards (for instance, gaining sufficient space to prevent intermingling of materials, improving the air handling system, etc.). Since a company is aware of this situation in advance of the actual change-of-site supplemental application (that is, at least four months) and must clearly delineate how the move will result in increased assurance of manufacturing standards so that the Division can arrange for orderly processing and review.

The Branch CSO's recommendation:

The Expedited Review should be **GRANTED** since it meets criteria
signature James P. Hannan date 4/25/91

The Expedited Review should be **DENIED** since it meets none of the criteria. signature _____ date _____

The Supervisory Chemist's recommendation:

The Expedited Review should be **GRANTED.**
signature John B. Harrison date 4/25/91

The Expedited Review should be **DENIED.**
signature _____ date _____

The Director's recommendation:

The Expedited Review should be **GRANTED.**
signature R. G. Jones date 4/26/91

The Expedited Review should be **DENIED**
signature _____ date _____

Remarks:

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 5/7/91

NDA NUMBER: 62-756

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☑ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Primaxin
ADD-Vantage

FIRM NAME: Merck

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Dr. Ken Brown

TELEPHONE NO.: (215) 834-2958

Requested:

① Production mfg. instructions and batch records.

Suggested

① May want to request categorical exclusion (Envir. Impact) under 21 CFR 25.24 (c)(1)

② Changes in 5-006 (5/6/90) — 5-009 (4/17/91)

③ These changes probably applicable to 50-587 Primaxin I.V. and 50-630 Primaxin I.M.

④ Note 21 CFR 210.84 (d)(1) need at min ID test for raw materials.

Call back 5/13/91
Ron Salerno
(215) 834-2958
amplify comment -

SIGNATURE: Eric P. Duff (ERIC P. DUFF)

DIVISION: HFD-625

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 7/24/91

NDA NUMBER: 62-756/S-006,S-007

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☑ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Primaxin® ADD-Vantage

FIRM NAME: Merck

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Dr Ron Salerno, Assoc. Dir. Reg. Aff.

TELEPHONE NO.: (215) 834-2958

re Primaxin Supplement to provide alt. _____ to _____

Requested:

1) Establish spec./tests & in final bulk for _____

2) Provide Commitment to Supplement w/ revised prodn scale process for _____

3) re S-006 of 5/29/91 for _____

Add this change to present supplement _____

4) Submit these changes to 50-587 & 50-630

SIGNATURE: Eric P. Duffy [ERIC P. DUFFY]

DIVISION: HFD-635

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 8/13/91

NDA NUMBER: 62-756

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Primaxin

FIRM NAME: Merck

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Suvra Roy HFD-520

TELEPHONE NO.: 443-6714

Discussed MSD amendments to Primaxin supplements dealing w/ ——— substitutions, to provide alternates to ———

1) NDAs 50-587 & 50-630 are to be approved - firm to be requested to provide data on ——— from prodn runs; if ——— are found - specs/test are to be established. Data should be provided for both imipenem and cilastatin.

2) EPD indicated that telecon (7/24/91) requests were not met w/ latest amendments - require commitment to provide prodn scale process description.

3) Request for establishment of ——— specs/test not met. - will accept the ——— test data and establishment of specs if levels warrant - but need commitment pre-approval.

SIGNATURE: Eric P. Duffy [ERIC P. DUFFY]

DIVISION: HFD-635

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE - 1984-432-976/7126

RECORD OF TELEPHONE CONVERSATION/MEETING

DATE: 8/13/91

NDA NUMBER: 62-756

IND NUMBER:

TELECON/MEETING

INITIATED BY: ☐ APPLICANT/SPONSOR ☐ FDA

MADE: ☐ BY TELEPHONE ☐ IN PERSON

PRODUCT NAME: Primaxin

FIRM NAME: Merck

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD: Ron Salerno Associate Dir. Reg. Affairs

TELEPHONE NO.: (215) 884-2958

re Supplement S-009 for change of ——— to provide alternate to ———

1) Will accept commitment to provide data on ——— levels for both Primaxin components & establishment of specs & test if ——— is observed (- in accord w/ HFD-520 request) in prodn batches.
2) Need validated method to be submitted for ——— determination for both Primaxin components
3) Need commitment to provide prodn scale process description instructions when available.

SIGNATURE: Eric P. Duffy [ERIC P. DUFFY]

DIVISION: HFD-625

FORM FD 2587 (11/77)

ORIGINAL IND/NDA

U. S. GOVERNMENT PRINTING OFFICE-1984-432-976/7126

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756/S-006 and S-009

CORRESPONDENCE

S-006 ✓
REJ

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

KENNETH R. BROWN, M.D.
GROUP DIRECTOR
REGULATORY AFFAIRS BIOLOGICS

(215) 834-2552
(215) 661-5000

May 29, 1990

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch, HFD-235
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Harrison:

Supplemental Abbreviated New Drug Application: ANDA 62-756
PRIMAXIN® ADD-Vantage® (Imipenem-Cilastatin Sodium, MSD)

Pursuant to Section 505(b) of the Food Drug and Cosmetics Act and in accordance with 21 CFR 314.50 and 21 CFR 314.70(b), we submit, for your approval, a supplement to ANDA 62-756.

As indicated on the attached Form FDA 356h, this supplemental application provides for a change in Item 3 of the approved Abbreviated New Drug Application for PRIMAXIN® ADD-Vantage®.

This supplemental application provides for an alternate procedure in the manufacture of bulk drug substance imipenem as follows:

The alternative use of a preferred ———————————————. Table I provides quality data which show the bulk substance imipenem made by the alternate procedure is equivalent to the quality of material made by the approved procedure.

Also included in the attached updated Control and Manufacturing Data are revised raw material information and manufacturing description. Hand annotated pages of the approved method showing the change together with a clean copy containing the change are provided for ease of review.

000 9246

ORIGINAL

We consider the filing of this Supplemental Abbreviated New Drug Application to be a confidential matter, and request the Food and Drug Administration not to make its content, nor any future communications in regard to it, public without first obtaining written permission of Merck & Co., Inc. Questions regarding this supplemental application should be directed to Kenneth R. Brown, M.D. (215/834-2552) or, in his absence, to David W. Blois, Ph.D. (215/834-2304).

Sincerely yours,

K R Brown

Kenneth R. Brown, M.D.
Group Director
Regulatory Affairs, Biologics

WL/cat
4371H

Attachments

Certified No. P 290 815 309

SCY-007

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

RONALD A. SALERNO, PH.D.
ASSOCIATE DIRECTOR
REGULATORY AFFAIRS

(215) 834-2958
(215) 661-5000
FAX (215) 834-2962

April 17, 1991

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch, HFD-235
Division of Generic Drugs
Office of Drug Standards
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Dr. Harrison:

U

REQUEST FOR EXPEDITED REVIEW

Supplemental New Drug Application for:

ANDA 62-756: PRIMAXIN® I.V. Add-Vantage® (Imipenem-Cilastatin Sodium, MSD)

Reference is made to the applications listed above and to pending supplemental NDA 50-587/S-028 submitted May 29, 1990. These supplemental applications provide for alternative procedures in the manufacture of imipenem and cilastatin sodium. The purpose of these new procedures is to provide a method of manufacture that eliminates the use of ———

[ ]

Reference is also made to a phone conversation between Ms. K. Huntley and myself on March 14, 1991, regarding a request for an expedited review of pending supplemental NDA 50-587/S-028. Ms. Huntley recommended that we clearly state the reason for the expedited review.

We are requesting an expedited review of both the attached supplement and pending SNDA 50-587/S-028 in order to implement the alternative procedures (for synthesis of imipenem and ——— substitutes) as soon as possible in 1991. Rapid FDA approval will assist us in the removal of ———

Redacted 1 page(s)

of trade secret and/or

confidential commercial

information from

4/17/1991 MSD LETTER

In summary, Merck requests an expedited review of NDA 50-587, NDA 50-630, and ANDA 62-756 supplements for elimination of ———————— from the manufacturing processes of the drug substances imipenem and cilastatin sodium. Pursuant to Section 505(B) of the Food and Drug Cosmetic Act and in accordance with 21 CFR 314.70(b), we consider the filing of this supplemental new drug application to be a confidential matter and request the Food and Drug Administration not to make its content, nor any future communications in regard to it, public without first obtaining written permission of Merck & Co., Inc. Questions regarding this supplemental application should be directed to myself, or in my absence, Kenneth R. Brown, M.D. (215-834-2552).

Sincerely yours,

Ronald A. Salerno

Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Liaison

cmf/3663F
attachments
Federal Express No. 8888266085

Desk Copy: Ms. Kathryn Huntley, CSO, HFD-520, Parklawn Bldg, Rm 12B-03
CDER, 5600 Fishers Lane, Rockville, MD 20857
Federal Express No. 8888266096

Desk Copy: Murray Lumpkin, M.D., Director, HFD-520, CDER,
5600 Fishers Lane, Rockville, MD 20857
(Letter only)

NDA SUPPL AMENDMENT

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

RONALD A. SALERNO, PH.D.
ASSOCIATE DIRECTOR
REGULATORY AFFAIRS

(215) 834-2958
(215) 661-5000
FAX (215) 834-2962

June 21, 1991

NDA NO. _____ REF. NO. SCX-009 AC
NDA SUPPL FOR CHEMISTRY

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch
HFD-635, Room 17B-31
Division of Generic Drugs
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Harrison:

RESPONSE TO FDA REQUEST FOR INFORMATION UNDER EXPEDITED REVIEW

Supplemental New Drug Application
ANDA 62-756 [redacted]-009 PRIMAXIN® I.V. ADD-Vantage®

Cross-referenced Supplements:
NDA 50-587/S-028 [redacted]: PRIMAXIN® I.V.
NDA 50-630/S-001: PRIMAXIN® I.M.

Reference is made to the above listed supplements which request expedited review for alternate procedures in the manufacture of imipenem and cilastatin sodium that eliminates the use of [redacted]. Reference is also made to conversations I had with Dr. E. Duffy of the Generics Drug Division and Dr. S. Roy and Dr. R. Roberts of the Anti-Infectives Division on May 13, 1991, May 20, 1991 and May 21, 1991 regarding the coordination of expedited reviews from both Divisions.

Since the manufacturing changes to bulk drug substance imipenem, [redacted] and bulk drug substance cilistatin sodium apply to all three NDA's (ANDA 62-756 filed with the Generics Drug Division, NDA 50-587 and NDA 50-630 filed with the Anti-Infectives Division), Mr. Bona, CSO of the Anti-Infectives Division, will coordinate the review of these supplements between Divisions.

With the present submission of information, we are responding to issues raised from the review of Dr. Duffy on May 13, 1991 and from the review of Dr. Roy on May 21, 1991. The information requested is being submitted to both Divisions as recommended by Dr. Roy. The information submitted addresses: (1) categorical exclusion, (2) manufacturing instructions and batch procedures, (3) raw material specifications, and (4) raw material grade.

RECEIVED
JUN 24 1991
ORIGINAL GENERIC DRUGS

We are very appreciative of the priority review and enthusiastic cooperation of Drs. Duffy, Roy, Roberts and Mr. Bona. Your rapid review is critical to meet commitments made on the part of Merck & Co. to achieve a [redacted] in the manufacture of these products as soon as possible in 1991.

Questions regarding this supplemental information should be directed to myself (215/834-2958) or, in my absence, Kenneth R. Brown, M.D. (215/834-2552).

Sincerely yours,

Ronald A. Salerno

Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Affairs

ALS/cat
75H

Attachments

Federal Express No. 7902181140

Desk Copy: Dr. Eric Duffy, HFD-635, Room 234
Federal Express No. 7902181136

Letter Only: Dr. Suva Roy, HFD-520, Room 12B-03
Federal Express No. 7902181103

Dr. Rosemary Roberts, HFD-520, Room 12B-45
Federal Express No. 7902181114

Mr. Jim Bona, HFD-521, Room 12B-03
Federal Express No. 7902181125

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

RONALD A. SALERNO, PH.D.
ASSOCIATE DIRECTOR
REGULATORY AFFAIRS

(215) 834-2958
(215) 661-5000
FAX (215) 834-2962

July 31, 1991

ORIGINAL

SCX-009 Ac

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch
HFD-635, Room 17B-31
Division of Generic Drugs
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Harrison:

RESPONSE TO FDA REQUEST FOR INFORMATION UNDER EXPEDITED REVIEW

Supplemental New Drug Application
ANDA 62-756/S-006, S-009: Primaxin® I.V. ADD-Vantage®

Cross-Referenced Supplements:

NDA 50-587/S-028 ——— Primaxin® I.V.
NDA 50-630/S-001, S-003: Primaxin® I.M.

Reference is made to the above listed supplements which request expedited review for alternate procedures in the manufacture of imipenem and cilastatin sodium that eliminates the use of ———————————————————. Reference is also made to an amendment of information submitted June 21, 1991 that responded to issues raised from the review of Dr. Duffy on May 13, 1991 and from the review of Dr. Roy on May 21, 1991. The present submission of information was requested by Dr. Duffy in a phone conversation on July 24, 1991 with me. The information submitted addresses data on production scale manufacturing of cilastatin including tests for ———————.

Since the manufacturing changes to bulk drug substance imipenem, ——————————, and bulk drug substance cilistatin sodium apply to all three NDA's (ANDA 62-756 filed with the Generics Drug Division, NDA 50-587 and NDA 50-630 filed with the Anti-Infectives Division), Mr. Bona, CSO of the Anti-Infectives Division, is coordinating the review of these supplements between Divisions.

As requested by Dr. Duffy, a copy of the June 21, 1991 submission is enclosed to amend ANDA 62-756/S-006.

We are very appreciative of the priority review and enthusiastic cooperation of Dr. Duffy and Dr. Roy. Your rapid review is critical to meet commitments made on the part of Merck & Co. to achieve [redacted] in the manufacture of these products as soon as possible in 1991.

Questions regarding this supplemental information should be directed to myself (215/834-2958) or, in my absence, Kenneth R. Brown, M.D. (215/834-2552).

Sincerely yours,

Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Affairs

ALS/cat
75H

Attachments

Certified No. P 856 788 895

Desk Copy: HFD-635/ANDA 62-756/S-006
Certified No. 856 788 900

HFD-635/ANDA 62-756/S-009
Certified No. 856 788 901

Dr. Eric Duffy, HFD-635, Room 234, Metro Park North II
Certified No. P 856 788 893

Letter Only: Dr. Rosemary Roberts, HFD-520, Room 12B-45
Certified No. P 856 788 891

Dr. Suva Roy, HFD-520, Room 12B-45
Certified No. P 856 788 890

Mr. Jim Bona, HFD-521, Room 12B-03
Certified No. P 856 788 892

Ms. Maureen Dillon-Parker, HFD-520, Room 12B-45
Certified No. P 856 788 894

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

RONALD A. SALERNO, PH.D.
ASSOCIATE DIRECTOR
REGULATORY AFFAIRS

(215) 834-2958
(215) 661-5000
FAX (215) 834-2962

July 31, 1991

ORIGINAL

3C -006 AC

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch
HFD-635, Room 17B-31
Division of Generic Drugs
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Dear Mr. Harrison:

RESPONSE TO FDA REQUEST FOR INFORMATION UNDER EXPEDITED REVIEW

Supplemental New Drug Application
ANDA 62-756/S-006, S-009: Primaxin® I.V. ADD-Vantage®

Cross-Referenced Supplements:

NDA 50-587/S-028 ——— Primaxin® I.V.
NDA 50-630/S-001, S-003: Primaxin® I.M.

Reference is made to the above listed supplements which request expedited review for alternate procedures in the manufacture of imipenem and cilastatin sodium that eliminates the use of ——— Reference is also made to an amendment of information submitted June 21, 1991 that responded to issues raised from the review of Dr. Duffy on May 13, 1991 and from the review of Dr. Roy on May 21, 1991. The present submission of information was requested by Dr. Duffy in a phone conversation on July 24, 1991 with me. The information submitted addresses data on production scale manufacturing of cilastatin including tests for ———.

Since the manufacturing changes to bulk drug substance imipenem, ——— ———, and bulk drug substance cilistatin sodium apply to all three NDA's (ANDA 62-756 filed with the Generics Drug Division, NDA 50-587 and NDA 50-630 filed with the Anti-Infectives Division), Mr. Bona, CSO of the Anti-Infectives Division, is coordinating the review of these supplements between Divisions.

As requested by Dr. Duffy, a copy of the June 21, 1991 submission is enclosed to amend ANDA 62-756/S-006.

Signed 8/2/91

We are very appreciative of the priority review and enthusiastic cooperation of Dr. Duffy and Dr. Roy. Your rapid review is critical to meet commitments made on the part of Merck & Co. to achieve a _____ in the manufacture of these products as soon as possible in 1991.

Questions regarding this supplemental information should be directed to myself (215/834-2958) or, in my absence, Kenneth R. Brown, M.D. (215/834-2552).

Sincerely yours,

Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Affairs

ALS/cat
75H

Attachments

Certified No. P 856 788 895

Desk Copy: HFD-635/ANDA 62-756/S-006
Certified No. 856 788 900

HFD-635/ANDA 62-756/S-009
Certified No. 856 788 901

Dr. Eric Duffy, HFD-635, Room 234, Metro Park North II
Certified No. P 856 788 893

Letter Only: Dr. Rosemary Roberts, HFD-520, Room 12B-45
Certified No. P 856 788 891

Dr. Suva Roy, HFD-520, Room 12B-45
Certified No. P 856 788 890

Mr. Jim Bona, HFD-521, Room 12B-03
Certified No. P 856 788 892

Ms. Maureen Dillon-Parker, HFD-520, Room 12B-45
Certified No. P 856 788 894

MERCK SHARP & DOHME RESEARCH LABORATORIES
DIVISION OF MERCK & CO., INC.
WEST POINT, PENNSYLVANIA 19486

RONALD A. SALERNO, PH.D.
ASSOCIATE DIRECTOR
REGULATORY AFFAIRS

(215) 834-2958
(215) 661-5000
FAX (215) 834-2962

Drug

August 21, 1991

AC
NDA SUPPL AMENDMENT SC-006
~~NDA ORIG AMENDMENT~~

RECEIVED
SEP 0 3 1991

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branch
HFD-635, Room 150
Division of Generic Drugs
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, Maryland 20855

AC
SCX-009
NDA SUPPL AMENDMENT

Dear Mr. Harrison:

RESPONSE TO FDA REQUEST FOR INFORMATION UNDER EXPEDITED REVIEW

Supplemental New Drug Application
~~ANDA 62-756/S-006, S-009 Primaxin® I.V. ADD-Vantage®~~

Cross-Referenced Supplements:

NDA 50-587/S-028 ——— Primaxin® I.V.
NDA 50-630/S-001, S-003: Primaxin® I.M.

Reference is made to the above listed supplements which request expedited review for alternate procedures in the manufacture of imipenem and cilastatin sodium that eliminates the use of ———————————————— ———————————.

The attached information is being submitted in response to a request by Dr. Duffy, in a phone conversation on August 14, 1991 with me, to document Merck's commitment to submit quality data (including tests for ———— ————) on three production lots of imipenem manufactured employing new procedures as soon as it is available. Also enclosed are detailed methods (including validation) for ———————— in imipenem sterile and cilastatin sodium.

Since the manufacturing changes to bulk drug substance imipenem, ———— ————————, and bulk drug substance cilistatin sodium apply to all three NDA's (ANDA 62-756 filed with the Generics Drug Division, NDA 50-587 and NDA 50-630 filed with the Anti-Infectives Division), Mr. Bona, CSO of the Anti-Infectives Division, is coordinating the review of these supplements between Divisions.

ORIGINAL

Questions regarding this supplemental information should be directed to myself (215/834-2958) or, in my absence, Kenneth R. Brown, M.D. (215/834-2552).

Sincerely yours,

Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Affairs

ALS/cat
75H

Attachments

Desk Copy: HFD-635/ANDA 62-756/S-006
HFD-635/ANDA 62-756/S-009
Dr. Eric Duffy, HFD-635, Room 150, Metro Park North II
Federal Express No. 0535961860

Letter Only: Dr. Suva Roy, HFD-520, Room 12B-45
Dr. Rosemary Roberts, HFD-520, Room 12B-45
Mr. Jim Bona, HFD-520, Room 12B-45
Ms. Maureen Dillon-Parker, HFD-520, Room 12B-45
Federal Express No. 0535961856

MERCK SHARP & DOHME RESEARCH LABORATORIES
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3.1

RONALD A. SALERNO, PH.D.
ASSOCIATE DIRECTOR
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September 4, 1991 ReSub. (8.21.91)

Mr. John D. Harrison, Chief
Antibiotic Drug Review Branc
HFD-635, Room 17B-31
Division of Generic Drugs
Office of Generic Drugs
Center for Drug Evaluation a
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

NDA SUPPL AMENDMENT
SC006 AC
SCX009 AC

Dear Mr. Harrison:

Supplemental New Drug Application
ANDA 62-756/S-006, S-009: Primaxin® I.V. ADD-Vantage®

Please refer to a telephone conversation on August 29, 1991 between Dr. Duffy and, in my absence, Dr. Bennett regarding our Supplemental New Drug Application (ANDA 62-756/S-006, S-009) dated August 21, 1991. In response to Dr. Duffy's request, we are resubmitting this supplemental application.

If you have any questions or need for additional information, please contact Ronald A. Salerno, Ph.D. (215/834-2958) or, in my absence, Kenneth R. Brown, M.D. (215/834-2552).

Sincerely yours,

Ronald A. Salerno

Ronald A. Salerno, Ph.D.
Associate Director
Regulatory Affairs

ALS/cat
75H

ORIGINAL

Attachments

Desk copies: HFD-635/ANDA 62-756/S-006
HFD-635/ANDA 62-756/S-009
Dr. Eric Duffy, HFD-635, Room 150, Metro Park North II
Federal Express No. 0535962114

RECEIVED
SEP 6 1991
GENERIC DRUGS