CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756 / S-033 and S-034

***Name*:** Primaxin® I.V. in ADD-Vantage® vials
(Imipenem and Cilastatin for Injection)

***Sponsor*:** Merck Research Laboratories

***Approval Date*:** October 11, 2001

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APPLICATION NUMBER:

ANDA 62-756 / S-033 and S-034

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APPLICATION NUMBER:

ANDA 62-756 / S-033 and S-034

APPROVAL LETTER

ANDA 62-756/S-033 & -034

OCT 11 2001

Merck & Co. Inc.
Attention: Virginia G. Snyder
P.O. Box 4
Sumneytown Pike, BLA-20
West Point, PA 19486

Dear Madam:

This is in reference to your supplemental new drug application, dated April 27, 2001, submitted under section 505 (j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for PRIMAXIN™ I.V. in ADD-Vantage™ Vials, 250 mg and 500 mg.

These supplemental applications, submitted as "Supplement Changes Being Effected in 30 Days", provide for the following changes:

S-033 an alternate stability testing site at the —— facility at ———— for imipenem.

S-034 an alternate HPLC test method for imipenem.

We have completed review of these supplemental applications and they are approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

The material submitted is being retained in our files.

Sincerely yours,

10/11/01

for

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 62-756/S-033 & -034
Division File
Field Copy

Endorsements:

HFD-643/RGanunis/9/21/01 Concurs 10/2/01

HFD-643/RAdams/9/27/01 R.C. adams 10/4/01

HFD-617/MAnderson/10/1/01 M Anderson 10/11/01

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F/T by rad10/01/01

APPROVAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-033 and S-034

CHEMISTRY REVIEWS

OFFICE OF GENERIC DRUGS
SUPPLEMENT REVIEW

ANDA 62-756/S-033 & -034

NAME AND ADDRESS OF APPLICANT
Merck & Co. Inc.
P.O. Box 4
Sumneytown Pike, BLA-20
West Point, PA 19486

PURPOSE OF SUPPLEMENT
The supplements provide for an alternate stability testing site at the —— facility in ———— for imipenem (S-033) and an alternate HPLC test method for the imipenem (S-034). These supplements qualify as CBE-30.

DATE OF SUBMISSION
April 27, 2001

PHARMACOLOGICAL CATEGORY
Antibacterial

TRADE NAME
PRIMAXIN™ I.V. in ADD-Vantage™ Vials

NONPROPRIETARY NAME
Imipenem-Cilastatin for Injection

DOSAGE FORM
Powder

STRENGTHS
250 mg and 500 mg

RX OR OTC
Rx

SAMPLES
N/A

RELATED IND/NDA/DMF
NDA 50-587, Primaxin™ IV

STERILIZATION
N/A

LABELING
N/A

BIOEQUIVALENCY STATUS
N/A

ESTABLISHMENT INSPECTION - Satisfactory
6/14/01

COMPONENTS/COMPOSITION/MANUFACTURING/CONTROLS - Satisfactory
These supplements were simultaneously submitted to the Division of Anti-Infective Drug Products for NDA 50-587. The review of the NDA supplements was completed by B.V. Shetty, and found approvable 7/10/01 (see attached).

PACKAGING
N/A

STABILITY
N/A

REMARKS AND CONCLUSION
Based on the approval recommendation by B. Vithal Shetty, Ph.D., for the supplements submitted for NDA 50-587, this supplement is recommended for approval.

RECALLS
N/A

REVIEWER
Ruth Ganunis

DATE COMPLETED
September 21, 2001

cc: ANDA 62-756/S-032 & -034
Division File
Field Copy

Endorsements:

HFD-643/RGanunis/9/21/01 Ganunis 10/2/01

HFD-643/RAdams/9/27/01 R.C. Adams 10/4/01

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F/T by rad10/1/01

APPROVAL

APPEARS THIS WAY
ON ORIGINAL

NDA 50-587/SCS-055

NDA SUPPLEMENT REVIEW

CHEMIST'S REVIEW 1	1. ORGANIZATION DAIDP (HFD-520)	NDA NUMBER 50-587

3. NAME & ADDRESS OF APPLICANT

Merck and Co Inc.
West Point,PA

4. AF NUMBER

5. SUPPLEMENT(S)

SCS-055 4/27/01_-_____

6. NAME OF DRUG
Primaxin IV

7. NONPROPRIETARY NAME
Cilastatin & Imipenem

8. SUPPLEMENT(s) PROVIDES FOR:
An alternate stability indicating HPLC method which will be used at an alternate testing site at ———————.for imipenem

9. AMENDMENTS AND OTHER(REPORTS, etc.) DATES

10. PHARMACOLOGICAL CATEGORY
Antibiotic

11. HOW DISPENSED
Rx XX OTC

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM(s)
I.V.

14. POTENCY(ies)

15. CHEMICAL NAME AND STRUCTURE

m.w.
CAS Registry No. - -
_REVIEWED

16. RECORDS AND REPORTS
CURRENT
x Yes X No
REVIEWED
Yes X No

17. COMMENTS
This drug is the subject of a compendial monograph, USP XXIV,page 411-cilastatin and page 863-imipenem. See items 29and35 for detailed comments.

18. CONCLUSIONS AND RECOMMENDATIONS:
Recommend approval letter to issue for this supplement.

Cc: Orig: NDA 50-587
HFD-520/Div File HFD-520/MO/Mulinde J
HFD-520/Pharm/Ellis HFD-520/CSO/Dillon-Parker

HFD-520/Shetty HFD-520/D. Katague:R/D initialed _

19 REVIEWER

NAME:B.Vithal Shetty,Ph.D.
SIGNATURE
DISTRIBUTION ORIGINAL JACKET REVIEWER
DATE COMPLETED 7/10/2001

20. Components and Composition: NA

21. Facilities and Personnel: NA

22. Synthesis:NA

23. Raw Material Controls: NA
    a. New Drug Substance
    b. Other Ingredients

24. Other Firms: NA

25. Manufacturing and Processing: NA

26. Container/Closure: NA

27. Packaging and Labeling: NA

28. Laboratory Controls (In-process and Finished Dosage Form): NA

29. Stability: ADEQUATE
The firm has submitted an alternative HPLC stability testing method which will be carried out at alternate testing site at the — facility, ———— for Primaxin IV injectable.
The HPLC method will be used as an alternate to the current assay method for stability testing. The firm has provided detailed description of the stability indicating method and corresponding validation. The firm states that the alternative testing facility is capable of performing the required stability. It is also stated that the facility in ———— was deemed acceptable for production of pharmaceutical products as per last satisfactory cGMP inspection dated ————.
The firm has also provided method equivalency testing data of three lots of bulk imipenem.

30. Control Numbers: NA

31. Samples and Results: NA

32. Labeling: NA

33. Establishment: NA

34. Recall: NA

35. Environmental Assessment: ADEQUATE.
The firm requests a categorical exclusion from the requirements of an Environmental Assessment under 21CFR 25.31(a) because it will not increase the use of the drug. To the best of the firm's knowledge, no extraordinary circumstances exist to this action.

15-JUN-2001

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application: NDA 50444/037 Priority: Org Code: 520
Stamp: 27-FEB-2001 Regulatory Due: 27-JUN-2001 Action Goal: District Goal: 23-MAY-2001

[redacted]

Overall Recommendation:
ACCEPTABLE on 15-JUN-2001 by S. FERGUSON (HFD-324) 301-827-0062

[redacted]

Reason: DISTRICT RECOMMENDATION
OBSER. NOT SIGNIFICANT ENOUG

[redacted]

Decision: ACCEPTABLE
Reason: DISTRICT RECOMMENDATION

APPEARS THIS WAY
ON ORIGINAL

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

B.V. Shetty
8/21/01 08:58:12 AM
CHEMIST

David Katague
8/21/01 09:24:59 AM
CHEMIST

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-033 and S-034

ADMINISTRATIVE DOCUMENTS

CBE- THIRTY (30) DAY SUPPLEMENT ROUTING FORM

This form is to accompany all CBE-30 Day supplements. Upon completion, return to the OGD Document Room

I. To be completed by the OGD Document Room using information from the applicant Cover letter:

DATE PROCESSED: 5/3/01
APPLICATION # : 62756 SUPPLEMENT # : SCB033AT SCS034 AT

II: To be determined by Chemistry Division Staff

Date and initial appropriate category. SPECIAL

Thirty (30) Day CBEs:

Chemistry Div. Staff	Qualifies as CBE-30 (GR)	Does Not Qualify. This is a CBE-0. (DC)	Does not Qualify. This is an Annual Report (DA)	Does not Qualify. This is a Prior Approval Supp. (DN)
Chemistry/Micro Project Manager(s)	MA 5/4/01			
Micro and/or Labeling Team Leader (as needed)				
Chemistry Team Leader	RCA 5/4/01			
Chemistry Div. Dir. Or Deputy* Dir.				

*Div/Deputy Director signature needed only when 1) CBE elevated to PAS or 2) PM/TM recommend different actions,

COMMENTS:

OK per ~~VIII~~ C.1(a)

III. To Project Manager Chemistry Team _____:

Prepare letter and notify applicant by telephone when CBE is denied because it is a prior approval supplement. DATE:_____

Notify applicant by telephone that inappropriate CBE category used. DATE _____

Request that applicant withdraw supplement when CBE qualifies for submssion as an Annual Report DATE _____

IV. To Document Room

Record appropriate CBE Code _____
File in archival submission

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-033 and S-034

CORRESPONDENCE

Virginia G. Snyder
Manager
Regulatory Affairs

Merck & Co., Inc.
P.O. Box 4, BLA-20
West Point PA 19486
Tel 610 397 7984
215 652 5000
Fax 610 397 2516

These copies are
OFFICIAL FDA Copies
not desk copies

ECR requested 5/15/01

April 27, 2001

Noted. To Redonda Adams M Anderson 5/19/01

Gary L. Buehler, Acting Director
Division of Generic Drug Products
Bldg. MPN2, HFD-600, Room 286 (CDER)
Food and Drug Administration
Metro Park North 2
7500 Standish Place
Rockville, Maryland 20855

MERCK
Research Laboratories

NDA NO. 62756 REF. NO. SCB032 AT
NDA SUPPL FOR Facility Add

BLA NO. REF NO. SCS034
NDA SUPPL FOR Control Rel AT OK per Dist C. 1.(a) 5/14/01 RDA

Dear Mr. Buehler:

AADA 62-756: PRIMAXIN™ IV in ADD-Vantage™ Vials
(Imipenem and Cilastatin for Injection)

SUPPLEMENT – CHANGES BEING EFFECTED IN 30 DAYS
PAC-ATLS: Post Approval Changes – Analytical Testing Laboratory Sites

Reference is made to the Abbreviated Antibiotic Drug Application (AADA) referenced above and to an April 25, 2001 telephone conversation between Ms. Susan Lange, OPS (Office of Pharmaceutical Sciences) and Ms. Virginia Snyder, MRL (a Division of Merck & Co., Inc.) in which it was agreed to bundle the CBE 30s for NDAs 50-587 PRIMAXIN™ IV for Injection, NDA 50-630 PRIMAXIN™ IM Injectable Suspension and AADA 62-756 PRIMAXIN™ IV in ADD-Vantage™ Vials. **As agreed, the supplement will be submitted simultaneously to the Anti-Infective Division for NDAs 50-587 and 50-630 and to this AADA 62-756 PRIMAXIN™ IV in ADD-Vantage™ Vials.**

Pursuant to Section 505(b) of the Food, Drug and Cosmetic Act and in accordance with 506A(d)(3)(B)(i) of the Food and Drug Administration Modernization Act, we submit, for the Agency's review and approval, a supplement to AADA 62-756.

This supplement provides for an alternate stability testing site at the ——facility at ——— for the imipenem. Additionally, this submission provides an alternate HPLC test method for imipenem.

As indicated on the attached Form FDA 356h, this supplemental application provides for changes in the *Chemistry* Section of the approved AADA for PRIMAXIN™ IV ADD-Vantage™ Vials.

CENTER FOR DRUG EVALUATION AND RESEARCH
MAY 0 1 2001
OGD

This submission includes the following items:

Chemistry, Manufacturing, and Control Documentation

A. Summary
B. List of References
   1. Summary of Test Methods and Acceptance Criteria for the Stability Testing of Imipenem
   2. Environmental Assessment
   3. Stability-Indicating Method for Assay
   4. Method Validation for Stability-Indicating Method for Assay

Merck & Co., Inc. is requesting a categorical exclusion for the requirements to prepare an Environmental Assessments under 21 CFR 25.31(a). This supplement meets the requirements of a categorical exclusion under 21 CFR 25.31(a) because it will not increase the use of the active moiety. To the best of the firm's knowledge, no extraordinary circumstances exist in regards to this action.

In accordance with the Prescription Drug User Fee Act of 1992 (PDUFA) and reauthorized in the Food and Drug Administration Modernization Act of 1997 (FDAMA), as indicated in the attached Form 3397, no user fee is required for this supplemental application.

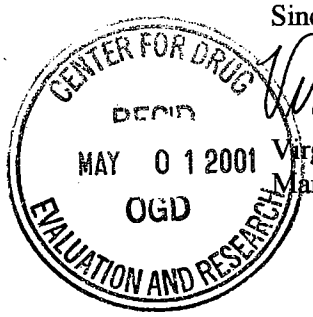
Pursuant to 21 CFR 314.50, a complete field copy of this supplement has been submitted to the FDA Philadelphia District Office.

As required by Section 306(k)(1) of the Generic Drug Enforcement Act [21 U.S.C. 335a (k)(1)], we hereby certify that, in connection with this application, Merck & Co., Inc. did not and will not use in any capacity the services of any person debarred under subsections 306 (a) or (b) of the Act.

We consider the filing of this Supplemental New Drug Application to be a confidential matter, and request that the Food and Drug Administration not make its content, nor any future communications in regard to it, public without first obtaining the written permission of Merck & Co., Inc.

Questions concerning this supplemental application should be directed to Virginia G. Snyder (610-397-7984) or, in my absence, to Dennis M. Erb, Ph.D. (610-397-7597).

Sincerely,



Virginia G. Snyder
Manager, Regulatory Affairs

Attachments

Federal Express #1

Desk copy: Mr. Mark Anderson, Senior Regulatory Project Manager (Cover Letter)
HFD-640, Rm. E251
Federal Express #2

Cover Letter only: Ms. Susan Lange, HFD-800, Rm. 13B31
Federal Express #3

Desk copy/att: Philadelphia District Office, FDA
Federal Express #4

Q:graz/chris/primaxin ADD CBE