CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756 / S-032

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

***Sponsor*:** Merck Research Laboratories

***Approval Date*:** September 10, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-032

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Reviews / Information Included in this Review	
Approval Letter	X
Tentative Approval Letter	
Labeling	
Labeling Reviews	
Medical Review(s)	
Chemistry Reviews	X
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Statistical Review(s)	
Microbiology Review(s)	
Administrative Documents	X
Correspondence	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-032

APPROVAL LETTER

ANDA 62-756/S-032

SEP 10 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 March 8, 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.

Reference is also made to your amendment dated March 22, 2001.

This supplemental application, submitted as "Supplement Changes Being Effected in 30 Days", provides for a change to the manufacturing process which allows for the [redacted] prior to filling.

We have completed review of this supplemental application and it is 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,

9/10/01

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

cc: ANDA 62-756/S-032
Division File
Field Copy
HFD-92

Endorsements:

HFD-643/RGanunis/8/30/01 RGanunis 9/6/01

HFD-643/RAdams/8/31/01 R.C - Adams 9/6/01

HFD-617/MAnderson/9/5/01 M Anderson 9/7/01

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F/T by rad9/6/01

APPROVAL

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-032

CHEMISTRY REVIEWS

OFFICE OF GENERIC DRUGS
SUPPLEMENT REVIEW

ANDA 62-756/S-032

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

PURPOSE OF SUPPLEMENT
Supplement-032 provides for a change to the manufacturing process for Primaxin IV. The change would allow for the [redacted] prior to filling as an alternate to filling performed [redacted]. This supplement was also submitted to the Division of Anti-Infective Drug Products for NDA 50-587. This supplement qualifies as a CBE-30.

DATE OF SUBMISSION
March 8, 2001 (electronic copy)
March 22, 2001 (hard copy)

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
N/A

COMPONENTS/COMPOSITION/MANUFACTURING/CONTROLS - Satisfactory
The firm plans to [redacted] This supplement was reviewed by the Division of Anti-Infective Drug Products for NDA 50-587, and was found acceptable (see attached).

PACKAGING
N/A

STABILITY
N/A

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

RECALLS
N/A

REVIEWER
Ruth Ganunis

DATE COMPLETED
August 29, 2001

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

Endorsements:

HFD-643/RGanunis/8/30/01 RGanunis 9/6/01

HFD-643/RAdams/8/31/01 R.C. Adams 9/6/01

V:\FIRMSAM\MERCK\LTRS&REV\62756s32apF.doc

F/T by rad9/6/01

APPROVAL

APPEARS THIS WAY
ON ORIGINAL

NDA 50-587/SCS-054

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) NUMBER(s) DATES CS-
SCS-054 2/15/01

6. NAME OF DRUG
Primaxin IV

7. NONPROPRIETARY NAME
Cilastin Sodium & Imipenem

8. SUPPLEMENT(s) PROVIDES FOR:
a change to the manufacturing process for Primaxin IV.The change would allow for the _____ prior to filling as an alternate to filling performed _____.

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)
Parenteral,IV

14. POTENCY(ies)
250mg,500mg vials

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-cilastin sodium and page 863-imipenem. See items 20-34 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/Pharm/
HFD-520/Shetty
HFD-520/MO/Moledina
HFD-520/CSO/Dillon-Parker
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

APPEARS THIS WAY
ON ORIGINAL

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: ADEQUATE

The firm plans to _____ prior to filling as an alternate to filling performed

26. Container/Closure: NA

27. Packaging and Labeling: NA

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

29. Stability: NA

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.

16-JUN-2001

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

[redacted]

[redacted]	J. CINTRON	(HFD-520)	301-827-2125 , Project Manager
	B. SHETTY	(HFD-520)	301-827-2187 , Review Chemist
	D. KATAGUE	(HFD-520)	301-827-2174 , Team Leader

Overall Recommendation:

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

[redacted]

Decision: ACCEPTABLE
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
7/11/01 01:45:29 PM
CHEMIST

David Katague
7/11/01 01:50:23 PM
CHEMIST

APPEARS THIS WAY
ON ORIGINAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-032

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: March 12, 2001
APPLICATION # : 62 752 SUPPLEMENT # : SCR-032/AP

II: To be determined by OGD Staff.

Date and initial appropriate category.

APPROVED

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)	3/29/01 MA			
Micro Team Leader (as needed)				
Chemistry Team Leader	4/9/01 RCA			

COMMENTS: Appears to fit under V.C.1.a
agree

III. To Project Manager Chemistry Team _____:

Prepare letter and notify applicnt 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

(revised 5/31/00)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-032

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

March 8, 2001

Central Document Room
Food and Drug Administration
Center for Drug Evaluation and Research
12229 Wilkins Avenue
Rockville, Maryland 20852

NDA NO. 62-756 REF NO. SCR 032/1
NDA SUPPL FOR Manufacturing Rev.

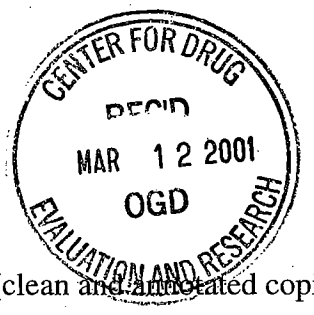
AADA 62-756: PRIMAXIN™ IV in ADD-Vantage™ Vials
(Imipenem and Cilastatin for Injection)

SPECIAL SUPPLEMENT – CHANGES BEING EFFECTED IN 30 DAYS

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 proposes a change to the manufacturing process for PRIMAXIN™ IV in ADD-Vantage™ Vials. The change would allow for the ——— prior to filling as an alternative to filling performed ———. It should be noted that a similar supplement for this manufacturing process changes was submitted on February 15, 2001 to the Division of Anti-Infective Drug Products for NDA 50-587. (SCS-054 in ◆)

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. All information is in an electronic format as indicated in the Table of Contents for this supplemental application. The Statement of Organization following this letter describes the sections contained in this application.



Attached on the CD are the following items:

Chemistry, Manufacturing and Control Documentation

A. Introduction
B. Categorical Exclusion for Environmental Assessment

List of Attachments:

1. Attachment 1: Product Manufacturing Description (clean and annotated copies)
2. Attachment 2: Validation Data for the ———
3. Attachment 3: ——— Validation
4. Attachment 4: Environmental Assessment – Categorical Exclusion

This supplemental application is formatted as required in Title 21 paragraph 314.50 of the Code of Federal Regulations and is being submitted in accordance with the January 1999, *Guidance for Industry – Providing Regulatory Submissions in Electronic Format – NDAs.* As an attachment to this letter, Merck Research Laboratories (MRL), a division of Merck & Co., Inc., is providing one Compact Disk (CD) which contains the supplemental application. All documents requiring signatures for certification are included as paper for archival purposes.

All of the information is contained on one CD and is not more than 100MB. We have taken precautions to insure that any software on the CD is free of computer viruses (Norton Anti-Virus 4.0, Symantec Corp., 1991-1997) and we authorized the use of anti-virus software as appropriate.

A list of reviewers from the Division of Anti-Infective Drug Products who should be provided access to this electronic submission on their desktops may be obtained from Mr. Mark Anderson, Regulatory Project Manager, Division of Generic Drug Products.

Merck & Co., Inc. is requesting a categorical exclusion for the requirements to prepare an Environmental Assessment 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

Enclosure: CD

Federal Express #1

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

Desk copy/att: Philadelphia District Office, FDA
Federal Express #3

Q:graz/chris/50587/primaxin CBE

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

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March 22, 2001

MERCK Research Laboratories

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

SUPPL AMENDMENT
SCR-032/AC

OK w CBE-30
4/9/01
RCA

Dear Mr. Buehler:

AADA 62-756/S-032: PRIMAXIN™ IV in ADD-Vantage™ Vials
(Imipenem and Cilastatin for Injection)

SPECIAL SUPPLEMENT – CHANGES BEING EFFECTED IN 30 DAYS

Reference is made to the Supplemental Abbreviated Antibiotic Drug Application (AADA) submitted on March 9, 2001. Additional reference is made to a telephone conversation on March 20, 2001 between Mr. Harvey Greenberg, FDA, and Ms. Virginia Snyder (MRL, a Division of Merck & Co., Inc.) during which the electronic submission of March 9, 2001 was discussed. Mr. Greenberg explained that the Generic Division did not have capabilities to accept supplemental applications electronically and requested that a hard copy of the submission be sent directly to the Generic Division. Further reference is made to a telephone conversation on March 20, 2001 between Mr. Mark Anderson (FDA) and Ms. Snyder during which Mr. Anderson acknowledged that the submission was logged in on March 12, 2001 and assigned supplement number S-032. It was agreed that the identical supplement would be resubmitted in hard copy for the Division of Generic Drug Products.

By copy of the letter, we are submitting the supplemental AADA (S-032) in hard copy.

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).

CENTER FOR DRUG EVALUATION AND RESEARCH
RECD
MAR 23 2001
OGD

Sincerely,

Virginia G. Snyder

Virginia G. Snyder
Manager, Regulatory Affairs

Federal Express #1

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

Q:graz/chris/50587/primaxin ADD-Vantage