CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 62-756 / S-027

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

***Sponsor*:** Merck Research Laboratories

***Approval Date*:** October 31, 1996

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APPLICATION NUMBER:

ANDA 62-756 / S-027

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APPLICATION NUMBER:

ANDA 62-756 / S-027

APPROVAL LETTER

AADA 62-756/S-027

Merck Research Laboratories
Attention: Henrietta N. Ukwu
Sumneytown Pike
West Point, PA 19486

OCT 31 1996

Dear Madam:

This is in reference to your supplemental antibiotic drug application dated August 6, 1996, submitted pursuant to 21 CFR 314.70(c,) regarding your abbreviated antibiotic drug application for PRIMAXIN® I.V.(Imipenem-Cilastatin Sodium for Injection) ADD-Vantage® Vials.

The supplement provides for the switch from the use of in-house manufactured ———————— to material purchased from an outside vendor (————————).

We have completed the review of this supplemental application and it is approved.

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

The material submitted is being retained in our files.

Sincerely yours,

10/31/96

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

cc: AADA 62-756/S027
Division File
FIELD COPY
HFD-600/Reading File
HFD-82/

Endorsements:
HFD-643/JClark/10-16-96 10-28-96
HFD-643/JHarrison/10-18-96 10/28/96
HFD-617/BWest/10-22-96 10/28/96

F/T by pah/10-28-96
x: new firmsam merck ltrs&rev 62756s027

APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-027

CHEMISTRY REVIEW

1. CHEMISTRY SUPPLEMENT REVIEW 2. AADA **62-756/S-027**

3. NAME AND ADDRESS OF APPLICANT
Merck Research Laboratories
Attention: Henrietta N. Ukwu
Sumneytown Pike
West Point, PA 19486

4. LEGAL BASIS FOR SUBMISSION 21 CFR 314.70

5. SUPPLEMENT(s) S-027

6. PROPRIETARY NAME **Primaxin® Add-Vantage® Vials.**

7. NONPROPRIETARY NAME
Imipenem-Cilastatin Sodium for Injection.

8. SUPPLEMENT(s) PROVIDE(s) FOR:
The supplement profices for the switch from the use of in-house manufactured [redacted] to material purchased from an outside vendor ([redacted]).

9. AMENDMENTS AND OTHER DATES:
August 6, 1996 Initial submission.

10. PHARMACOLOGICAL CATEGORY
antibiotic

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM Injection-I.V.

14. POTENCY **250mg/250mg**
500mg/500mg

15. CHEMICAL NAME AND STRUCTURE
As per USAN.

16. RECORDS AND REPORTS N/A

17. COMMENTS

[redacted]

18. CONCLUSIONS AND RECOMMENDATIONS Approve supplement S-027

19. REVIEWER: Jon E. Clark DATE COMPLETED: October 16, 1996

20. COMPONENTS AND COMPOSITION — no change

21. FACILITIES AND PERSONNEL — no change

22. SYNTHESIS — no change

[redacted]

23. RAW MATERIAL CONTROLS — no change

[redacted]

24. OTHER FIRM(s) — no change

25. MANUFACTURING AND PROCESSING — no change

26. CONTAINER — no change

27. PACKAGING AND LABELING — no change

28. LABORATORY CONTROLS (IN-PROCESS AND FINISHED DOSAGE FORM)
no change

Data is provided comparing the product manufactured using the ——— prepared in-house with the ——— that is purchases. The data are equivalent.

29. STABILITY — no change

No stability data is needed for the approval of this supplement. None is provided.

30. CONTROL NUMBERS — N/A

31. SAMPLES AND RESULTS — N/A

32. LABELING — no change

33. ESTABLISHMENT INSPECTION — N/A

34. BIOEQUIVALENCY STATUS — N/A

35. ENVIRONMENTAL IMPACT CONSIDERATIONS/CATEGORICAL EXCLUSION:
N/A

36. ORDER OF REVIEW: The application submission(s) covered by this review was taken in the date order of receipt Yes___X___

cc: AADA 62-756/S-027
Division File
FIELD COPY

Endorsements:
HFD-643/JClark/10-16-96 Jan E Clark 10-28-96
HFD-643/JHarrison/10-16-96 J Harrison 10/28/96
X:\new\firmsam\merck\ltrs&rev\62756s27.apf

APPEARS THIS WAY
ON ORIGINAL

37. **DMF CHECKLIST FOR AADA # 62-756 REVIEW # 1**

DMF #	DMF TYPE/SUBJECT/HOLDER	ACTION CODE	RESULT OF REVIEW	DATE REVIEW COMPLETED
———	I/————————————	2		

Comments: No DMF references are made in this submission.

Comments:

Comments:

Comments:

Comments:

Comments:

Comments:

Comments:

APPEARS THIS WAY ON ORIGINAL

ACTION CODES: (1) DMF Reviewed. Other codes indicate why the DMF was not reviewed, as follows:

(2) Type 1 DMF;
(3) Reviewed previously and no relevant revision since last review;
(4) Sufficient information in application;
(5) Authority to reference not granted;
(6) DMF not available;
(7) Other (explain under"Comments").

Checklist page 1 of 1 .

Jon E. Clark		
Reviewer	Signature	Date

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-027

ADMINISTRATIVE DOCUMENTS

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: September 23 1996

FROM: Robert L. West , Consumer Safety Officer

SUBJECT: Special Supplement - Changes Placed into Effect

TO: Document Room

Please make the following entry in the MIS concerning the status of this Special Supplement - Changes Placed into Effect.

ANDA(s)	SUPPLEMENTS(s)	APPL	GRANTED	DENIED
62-756	S-027	HSD	J. Harrison 9/23/96	

Primaxin I.V.

This form is to accompany the action package/jacket.

Thank you,

Robert L. West 9/23/96
Signature of CSO and Date

cc:

ANDA
DIVISION FILE

7.1

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 62-756 / S-027

CORRESPONDENCE

Henrietta N. Ukwu, M.D.
Director
Regulatory Liaison

These copies are OFFICIAL FDA Copies
not desk copies.

Merck & Co., Inc.
P.O. Box 4, BLA-30A
West Point PA 19486-0004
Fax 610 397 2962
Tel 610 397 7176
215 652 5000

August 6, 1996

Mr. John D. Harrison, Chief
Office of Generic Drugs
HFD-635, Room NPN2
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

RECEIVED
AUG 0 9 1996
GENERIC DRUGS

MERCK
Research Laboratories

NDA NO. _____ REF NO. SC-027
NDA SUPPL FOR MAN47/54pp.
SC-027/Ai

Dear Mr. Harrison:

SPECIAL SUPPLEMENT - CHANGES BEING EFFECTED

AADA 62-756: PRIMAXIN I.V.® in ADD-Vantage® Vials
(Imipenem-Cilastatin Sodium for Injection)

Pursuant to Section 505(b) of the Food Drug and Cosmetic Act and in accordance with 21 CFR 314.70 (c)(3) we submit a supplement to AADA 62-756.

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

This supplement provides for the switch from use of in-house manufactured ———————, a key raw material used in the synthesis of active ingredient imipenem, to material purchased from an outside vendor (———————).

To support the change, the following attachments described below are included:

- **Attachment 1 - Test Data on Merck Manufactured and Purchased ———————**
  Quality data on three batches of — manufactured by Merck and three batches manufactured at production scale by — are presented in a tabular format. The data demonstrate that material manufactured by — is comparable to that currently manufactured by Merck Manufacturing Division.

- **Attachment 2 - Test Data on Imipenem Nonsterile Manufactured Using Both Merck and Purchased —**
  Quality data are presented in a tabular format on two test batches of imipenem prepared using — from our proposed supplier, as well as data on a control batch made using in-house manufactured —. Each batch was manufactured on a laboratory scale under non-sterile conditions.

- **Attachment 3 - *Raw Materials - Tests and Expected Values***
  Hand-annotated and clean copies of a revised listing of imipenem *Raw Materials - Tests and Expected Values* are included. The listing has been revised to show the tests and expected values adopted for purchased ———————

- **Attachment 4 - Imipenem Sterile Process Description**
  Hand-annotated and clean copies of a revised imipenem sterile process description are included. The description is revised with respect to the preparation of [redacted], to indicate that this compound is prepared via the described process either in-house or by an outside vendor.

- **Attachment 5 - Listing of Manufacturing Sites**
  Included is a revised listing of manufacturing sites to include [redacted] for the manufacture of [redacted] in the imipenem sterile process.

- **Attachment 6 - Letter of Authorization from [redacted]**
  Included is a letter from [redacted] authorizing FDA to examine their DMF on behalf of Merck & Co., Inc. in connection with supplemental filings related to [redacted]

The changes will become effective on or about December 1, 1996 and will apply to all packages of PRIMAXIN I.V.® in ADD-Vantage® Vials distributed from the company's manufacturing facilities at West Point, PA.

As required by Section 306(k)(1) of the Generic 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.

Pursuant to 21 CFR 314.70(a), a complete field copy of this supplement has been submitted to the FDA Philadelphia district Office.

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 the written permission of Merck & Co., Inc.

Questions concerning this supplemental application should be directed to Henrietta N. Ukwu M.D. (610/397-7176) or, in my absence Bonnie J. Goldmann, M.D. (610/397-2383).

Sincerely yours,

Henrietta Ukwu, M.D.
Director
Regulatory Liaison

Attachments

Certified No. P 914 184 626
Q/YARB/SARF/LTR/BFI-2

Desk Copy: Philadelphia District Office, Food and Drug Administration Room 900
U.S. Custom House, 2nd & Chestnut Streets, Philadelphia, PA 19106-2973
Certified No. P 914 184 627