CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75-684

CORRESPONDENCE

BEDFORD
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505
(j)(2)(A)

July 30, 1999

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: Abbreviated New Drug Application
PRODUCT: Famotidine Injection, 10 mg/mL, 50 mL per vial Pharmacy Bulk

Dear Sir/Madam:

In accordance with Section 505 (j) (1) of the Federal Food, Drug and Cosmetic Act, Bedford Laboratories is submitting in triplicate (an archival copy, a review copy and a field copy) an Abbreviated New Drug Application for Famotidine Injection, 10 mg/mL; 50 mL vial Pharmacy Bulk. Please note that the field copy has been sent directly to the FDA District Office in Cincinnati, Ohio.

The drug product subject to this application will be manufactured by Ben Venue Laboratories, Inc., located at 270 Northfield Road, Bedford, Ohio, 44146.

This abbreviated new drug application contains the information required by Section 505 (j)(2)(A)(i), (ii)(I), (iv), (v) and (vi). The application is provided in the format suggested by your office, (Guidance for Industry, "Organization of an ANDA," OGD #1, Revised February 1999), and contains a copy of the package insert of the "listed drug" (Merck & Co., Inc, Pepcid® Injection.) and a copy of the approved citizen's petition submitted by Marsam Pharmaceuticals, Inc. Docket no. 97P-0011/CP1, Famotidine Injection Pharmacy Bulk. This application consists of three volumes.

In accordance with Title 21 CFR 320.22 Bedford Laboratories requests a waiver of the requirement for submission of evidence demonstrating the *in vivo* bioavailability/bioequivalence for the drug product that is the subject of our application (Famotidine Injection, 10 mg/mL; 50 mL per vial). The drug product is a solution intended solely for intravenous administration and it contains the active ingredient in the same concentration as in the listed drug.

Bedford Laboratories certifies that the methods used in, and the facilities and controls used for the manufacture, processing, packaging and holding of the drug product are in conformity with current Good Manufacturing Practices in accordance with Title 21 CFR 210 and 211. Ben Venue's signed statement is provided in Section IX (MANUFACTURING FACILITY) Subsection 3 (cGMP Certification).

Bedford Laboratories commits to provide full cooperation to resolve any problem which may arise during the methods validation testing as part of the "Post-Approval" process for the above listed drug product.

A DIVISION OF BEN VENUE LABORATORIES, INC.
300 Northfield Road • Bedford, Ohio 44146 • (440) 232-3320 • Fax (440) 232-6264

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Two copies of analytical methods which were used to test this product and an analytical method validation package are enclosed separately along with this application.

Section XXII of this application, located in Volume 3, contains the Sterilization Assurance Data and Information as well as the following: A copy of the labeling and package insert, a summary of the manufacturing process including the components and composition statement, and copies of the executed batch record containing holding times, filtration integrity testing and sterilization records.

If the Agency has any comments or further requests or if we could be of any assistance in your review, the phone numbers for contact are (440)-232-3320, ext. 333 (direct) and (440)-439-6398 (fax).

Sincerely,
for Bedford Laboratories™

Shahid Ahmed
Director, Regulatory Affairs
Ben Venue Laboratories, Inc.

ANDA 75-684

Bedford Laboratories
A Division of Ben Venue Laboratories, Inc.
Attention: Shahid Ahmed
270 Northfield Road
Bedford, OH 44146

SEP 24 1999

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.

NAME OF DRUG: Famotidine Injection, 10 mg/mL, 50 mL vial, Pharmacy Bulk Package

DATE OF APPLICATION: July 30, 1999

DATE (RECEIVED) ACCEPTABLE FOR FILING: August 03, 1999

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:

Kassandra Sherrod
Project Manager
(301) 827-5848

Sincerely yours,

/s/

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

MAJOR AMENDMENT

FEB 2 200

ANDA 75-684

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Bedford Laboratories PHONE: 440-232-3320 ext. 333

ATTN: Shahid Ahmed FAX: 440-439-6398

FROM: Kassandra Sherrod PROJECT MANAGER (301) 827-5849

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated July 30, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Famotidine Injection, 10 mg/mL.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR AMENDMENT should appear prominently in your cover letter. You have been notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

Chemistry, labeling and bioequivalence comments. jms

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MESSAGE CONFIRMATION

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MAJOR AMENDMENT

FEB 2 2000

ANDA 75-684

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Bedford Laboratories PHONE: 440-232-3320 ext. 333

ATTN: Shahid Ahmed FAX: 440-439-6398

FROM: Kassandra Sherrod PROJECT MANAGER (301) 827-5849

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated July 30, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Famotidine Injection, 10 mg/mL.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

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February 28, 2000

Major Amendment / Chemistry and Labeling Deficiency

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park II
7500 Standish Place, Room 150
Rockville, MD 20855

NDA ORIG AMENDMENT
N/AC

RE: **ANDA 75-684/Major Amendment**
Product: **Famotidine Injection; 10 mg/mL, 50 mL per vial Pharmacy Bulk**

Dear Sir/Madame:

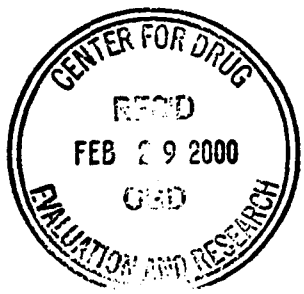
We wish to amend our unapproved Abbreviated New Drug Application, ANDA 75-684, for Famotidine Injection, 10 mg/mL, 50 mL per vial Pharmacy Bulk to remove the deficiencies cited in the Major Deficiency of February 2, 2000.

The number associated with the response given below corresponds to the number identifying the deficiencies in the communication. Form 356H is provided in Attachment I.

A. Chemistry Deficiencies:

1. Bedford Laboratories™ acknowledges that the active drug substance is an official article in the USP, and in the event of a dispute, the results obtained by the official method and procedures in the USP will be considered conclusive.

[redacted]



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1 page has been withheld in full from this document.

B. ACKNOWLEDGEMENTS

1. Bedford Laboratories™ acknowledges that the evaluation of our method by the Detroit District Laboratory is still pending.

C. LABELING

1. All deficiencies cited have been corrected. Please refer to Attachment X for twelve copies of final printed vial labels, carton and package insert labeling for review. Also located in Attachment X are annotated side-by-side comparisons of the final printed package insert with the last draft package insert.

BEDFORD
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We trust this meets with your approval. If there are any questions or comments, please call the undersigned at (440)232-3320, ext. 333, for any additional information.

Sincerely,
for Bedford Laboratories™

Shahid Ahmed
Director, Regulatory Affairs
Ben Venue Laboratories, Inc.

BEDFORD
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June 13, 2000

Chemistry Amendment

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park II
7500 Standish Place, Room 150
Rockville, MD 20855

NDA ORIG AMENDMENT
N/Ac

RE: ANDA 75-684/Chemistry Amendment
Product: Famotidine Injection; 10 mg/mL, 50 mL per vial

Dear Sir/Madame:

We wish to amend our unapproved Abbreviated New Drug Application, ANDA 75-684, for Famotidine Injection, 10 mg/mL, 50 mL per vial. FDA Form 356h is provided in Attachment I. The DMF holder — was found deficient by the Agency during the review of ANDA 75-622 (Bedford Laboratories™), and has now responded to those deficiencies. A copy of the response letter is provided in Attachment II.

We trust this meets with your approval. If there are any questions or comments, please call the undersigned at (440)232-3320, ext. 333, for any additional information.

Sincerely,
for Bedford Laboratories™

Shahid Ahmed
Director, Regulatory Affairs
Ben Venue Laboratories, Inc.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUN 14 2000
OGD

A DIVISION OF BEN VENUE LABORATORIES, INC.
300 Northfield Road • Bedford, Ohio 44146 • (440) 232-3320 • Fax (440) 232-6264

MINOR AMENDMENT

AUG 10 2000

ANDA 75-684

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Bedford Laboratories PHONE: 440-232-3320 ext333

ATTN: Shahid Ahmed FAX: 440-232-2772

FROM: Kassandra Sherrod PROJECT MANAGER (301) 827–5849

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated July 30, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Famotidine Injection, 10 mg/mL, 50 mL Pharmacy Bulk Package.

Reference is also made to your amendment(s) dated February 28 and June 13, 2000.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (4 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry and labeling deficiencies and microbiology deficiencies

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MESSAGE CONFIRMATION

08/10/00 13:32
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DATE	S.R-TIME	DISTANT STATION ID	MODE	PAGES	RESULT	
08/10	01'41"	4402322772	CALLING	05	OK	0000

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MINOR AMENDMENT

AUG 10 2000

ANDA 75-684

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

TO: APPLICANT: Bedford Laboratories PHONE: 440-232-3320 ext333

ATTN: Shahid Ahmed FAX: 440-232-2772

FROM: Kassandra Sherrod PROJECT MANAGER (301) 827-5849

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated July 30, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Famotidine Injection, 10 mg/mL, 50 mL Pharmacy Bulk Package.

Reference is also made to your amendment(s) dated February 28 and June 13, 2000.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (1 pages). This facsimile is to be regarded as an official FDA

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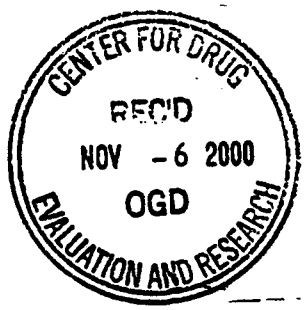
NDA ORIG AMENDMENT
N/AM

November 3, 2000

Minor Amendment
Chemistry and Microbiology Deficiencies

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park II
7500 Standish Place, Room 150
Rockville, MD 20855



RE: **ANDA 75-684/Minor Amendment**
Product: **Famotidine Injection; 10 mg/mL, 50 mL per vial**

Dear Sir/Madame:

We wish to amend our unapproved Abbreviated New Drug Application, ANDA 75-684, for Famotidine Injection, 10 mg/mL, 4 mL and 20 mL per vial. FDA Form 356h is provided in Attachment I.

A. CHEMISTRY DEFICIENCY

[redacted]

11-8-00

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2 pages have been withheld in full from this document.

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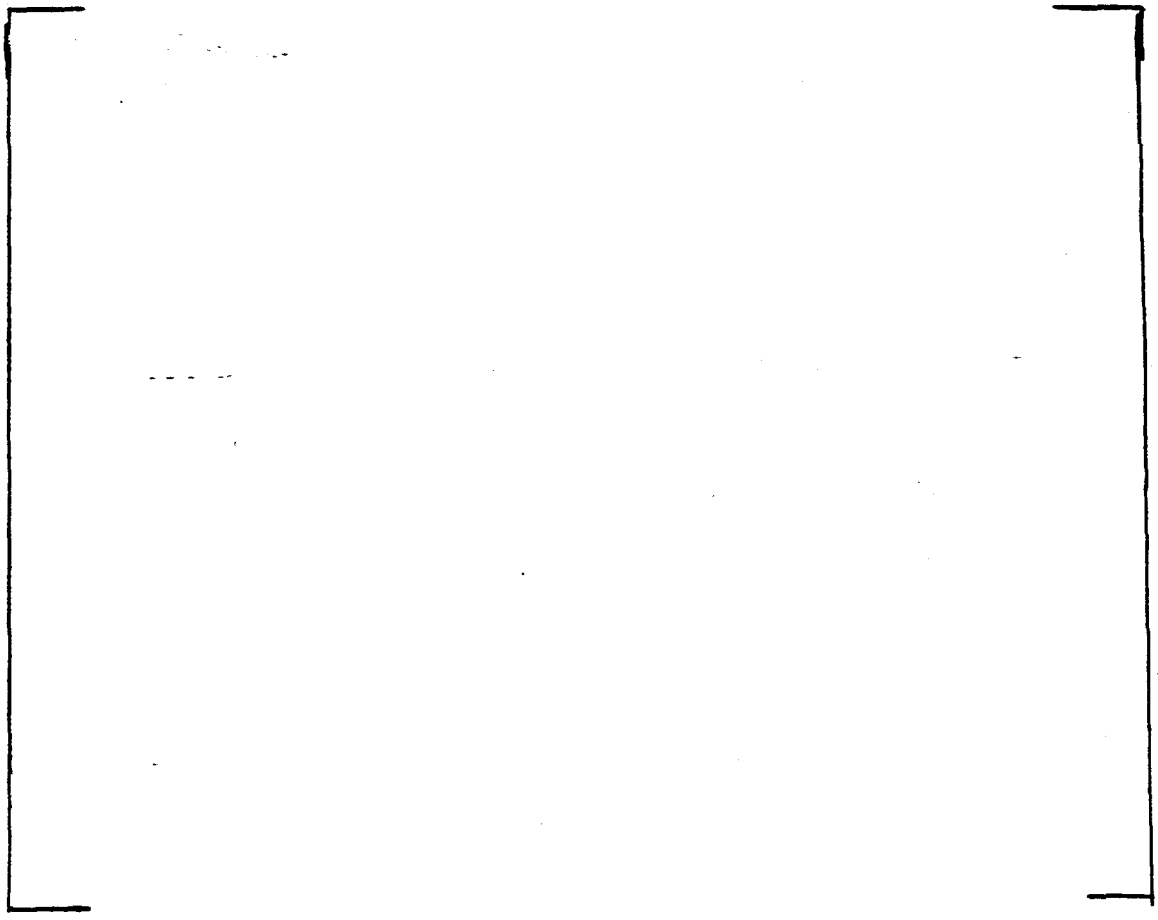
B. MICROBIOLOGY DEFICIENCIES



C. LABELING DEFICIENCIES

The container label, carton, and package insert labeling have been revised in accordance with the deficiency comments. A side by side comparison is provided in Attachment IX. Twelve copies of the final printed labeling are also included in Attachment IX.

We trust this meets with your approval. If there are any questions or comments, please call the undersigned at (440)232-3320, ext. 3333, for any additional information.

Sincerely,
for Bedford Laboratories™

Shahid Ahmed
Vice President, Regulatory Affairs
Ben Venue Laboratories, Inc.

BEDFORD LABORATORIES™

ORIG AMENDMENT

N/AM

December 1, 2000

Telephone Amendment/Chemistry

Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park II
7500 Standish Place, Room 150
Rockville, MD 20855

RE: **ANDA 75-684/ Telephone Amendment**
Product: **Famotidine Injection; 10 mg/mL, 50mL per vial**

Dear Sir/Madame:

We wish to amend our unapproved Abbreviated New Drug Application, ANDA 75-684, for Famotidine Injection, 10 mg/mL, 50 mL per vial, in accordance with a telephone discussion with Mr. Raymond Brown from the Agency and Ms. Pratima Patel and Ms. Molly Rapp from Ben Venue Laboratories. Form 356H is provided.

The drug substance chromatographic purity method has also been revised to include the Relative Retention time of this impurity for identification and quantitation purposes. The revised specification and method are attached for your review.

In addition, the Statement of Exclusivity has been revised to reflect the Pediatric Exclusivity Period granted to the Reference Listed Drug, which will expire on April 15, 2001. The revised statement is attached.

Sincerely,
for Bedford Laboratories™

Shahid Ahmed
Vice President, Regulatory Affairs
Ben Venue Laboratories, Inc.

A DIVISION OF BEN VENUE LABORATORIES, INC.

300 Northfield Road • Bedford, Ohio 44146 • (440) 232-3320 • Fax (440) 232-6264

ANDA 75-684

JAN 24 2001

Bedford Laboratories
Attention: Shahid Ahmed
270 Northfield Road
Bedford, Ohio 44146

Dear Sir:

This is in reference to your abbreviated new drug application dated July 30, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Famotidine Injection, 10 mg/mL, supplied in 50 mL Pharmacy Bulk Packages.

Reference is made to your amendments dated November 3, December 1, and December 22, 2000.

We have completed the review of this abbreviated application and have concluded that based upon the information you have presented to date, the drug is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved.** This determination is based upon information available to the Agency at this time, (i.e., information in your application and the status of current good manufacturing practices (CGMP) of the facilities used in the manufacture and testing of the drug product). Please note that this decision is subject to change on the basis of new information that may come to our attention.

The reference listed drug product (RLD) upon which you have based your application, Pepcid Injection of Merck Research Laboratories, is subject to a period of patent protection (U.S. Patent No. 4,283,408. Your application contains a Paragraph III Certification to this patent under Section 505(j)(2)(A)(vii)(III) of the Act stating that you will not market this drug product prior to patent expiry. Therefore, final approval of this application may not be made effective pursuant to 21 U.S.C. 355 (j)(5)(B)(ii) of the Act until this patent has expires, i.e., currently April 15, 2001.

Because the agency is granting a tentative approval to this application, please submit an amendment at least 60 days prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final printed labeling, chemistry, manufacturing, and/or controls data as appropriate. In order to reactivate your application prior to final approval, an amendment should be submitted even if none of these changes were made. This amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. In addition to this amendment, the Agency may request at any time prior to the final date of approval that you submit an additional amendment containing the information described above.

Failure to submit either amendment may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application, as well as changes in the status of the manufacturing and testing facilities' compliance with current good manufacturing practices (CGMPs) are subject to agency review before final approval of the application will be made.

Please note that this drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 311(d). Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book"), published by the Agency. Should you believe that there is a basis for issuing the final approval letter prior to April 15, 2001, you should amend your application accordingly.

If you have questions concerning the status of this application, please contact Kassandra Sherrod, R.Ph., Project Manager, at (301) 827-5849.

Sincerely yours,

/S/

Gary Buehler 1/24/01
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research