CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 074531Orig1s001

Name: Fluphenazine Decanoate Injection USP
25 mg/mL

Sponsor: Bedford Laboratories

Approval Date: April 3, 2001

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 074531Orig1s001

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 074531Orig1s001

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

ANDAs (See Attachment)

Food and Drug Administration
Rockville MD 20857

Bedford Laboratories
Attention: Shahid Ahmed
300 Northfield Road
Bedford, OH 44146

APR 3

Dear Sir:

This refers to your supplemental new drug applications dated March 6, 2001 submitted under Section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding the products listed in the attachment.

These supplemental applications, submitted as "Supplement-Changes Being Effected", provide for the use of a new (b)(4) filling line at your facility.

We have completed the 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,

Mary Fanning, M.D., Ph.D.
Associate Director for Medical Affairs
Office of Generic Drugs
Center for Drug Evaluation and Research

Attachment

ANDA(s):	
72-323/SS-005	Acetylcysteine Injection, 10%; 10mL and 30 mL vials
72-324/SS-005	Acetylcysteine Injection, 20%; 10mL and 30 mL vials
74-815/SS-004	Alprostadil Injection, USP; 0.5 mg/mL, 1 mL vials
63-313/SS-003	Amikacin Sulfate Injection, USP; 50 mg/mL, 2mL vials
75-513/SS-001	Inamrinone Injection; 5 mg/mL, 20mL vials
63-315/SS-002	Amikacin Sulfate Injection, USP; 250 mg/mL, 2mL and 4mL vials
74-900/SS-002	Atracurium Besylate Injection; 10 mg/mL, 2.5 mL and 5 mL vials
74-901/SS-002	Atracurium Besylate Injection, Preserved; 10 mg/mL, 10 mL vials
74-441/SS-009	Bumetanide Injection, USP; 0.25 mg/mL, 2mL, 4 mL and 10 mL vials
75-045/SS-002	Butorphanol Tartrate Injection, USP; 1 mg/mL, 1mL vial; 2 mg/mL, 1mL and 2 mL vials
75-046/SS-002	Butorphanol Tartrate Injection, USP; 2 mg/mL, 10 mL vials
40-273/SS-001	Chloroprocaine Hydro-chloride Injection, USP; 20 mg/mL, 20mL vials and 30 mg/mL, 20 mL vials
75-405/SS-003	Cladribine Injection; 1 mg/mL, 8 mL and 10 mL vials

65-004/SS-002	Cyclosporine Injection, USP; 50 mg/mL, 5 mL vials
74-617/SS-010	Diltiazem Hydrochloride Injection; 5 mg/mL, 5 mL, 10 mL and 25 mL vials
74-939/SS-001	Dipyridamole Injection; 5 mg/mL, 2 mL and 10 mL vials
74-277/SS-012	Dobutamine Injection, USP; 12.5 mg/mL, 20 mL vials
62-975/SS-011	Doxorubicin Hydrochloride Injection, USP; 2 mg/mL, 5 mL, 10 mL and 20 mL vials
75-634/SS-001	Enalaprilat Injection; 1.25 mg/mL, 1 mL and 2 mL vials
74-593/SS-002	Etomide Injection; 2 mg/mL, 10 mL and 20 mL vials
74-290/SS-010	Etoposide Injection; 20 mg/mL, 5 mL, 25 mL and 50 mL vials
74-531/SS-001	Fluphenazine Decanoate Injection, USP; 25mg/mL, 5mL vials
81-066/SS-002	Folic Acid Injection, USP; 5 mg/mL, 10 mL
74-811/SS-002	Haloperidol Decanoate Injection, USP; 50 mg/mL, 1mL and 5mL vials
75-305/SS-002	Haloperidol Decanoate Injection, USP; 100 mg/mL, 1mL and 5mL vials
75-513/SS-001	Inamrinone Injection; 5 mg/mL, 20 mL vials
75-524/SS-003	Ketamine Hydrochloride Injection, USP; 50 mg/mL, 10 mL vials and 100 mg/mL, 5 mL vials

75-222/SS-001	Ketorolac Tromethamine Injection, USP; 15 mg/mL, 1 mL vials and 30 mg/mL, 1 mL and 2 mL vials
75-228/SS-001	Ketorolac Tromethamine Injection, USP; 30 mg/mL, 30 mL vials
75-303/SS-001	Labetalol Hydrochloride Injection, USP; 5 mg/mL, 20 mL and 40 mL vials
40-347/SS-001	Leucovorin Calcium Injection; 10 mg/mL, 30 mL and 50 mL vials
74-728/SS-002	Leuprolide Acetate Injection; 1 mg/mL, 0.2 mL vials
89-340/SS-021	Methotrexate Injection, USP; 25 mg/mL, 2 mL, 4mL, 8 mL and 10 mL vials
89-341/SS-021	Methotrexate Injection, USP; 25 mg/mL, 2 mL, 4mL, 8 mL and 10 mL vials
89-342/SS-021	Methotrexate Injection, USP; 25 mg/mL, 2 mL, 4mL, 8 mL and 10 mL vials
89-343/SS-021	Methotrexate Injection, USP; 25 mg/mL, 2 mL, 4mL, 8 mL and 10 mL vials
75-247/SS-001	Midazolam Hydrochloride Injection; 1 mg/mL, 2 mL, 5 mL, 10 mL vials 5 mg/mL, 1 mL, 2 mL, 5 mL and 10 mL vials
75-792/SS-001	Propranolol Hydrochloride Injection, USP; 1 mg/mL, 1 mL vials
75-421/SS-001	Midazolam Hydrochloride Injection, USP; 1 mg/mL, 5 mg/mL

CC: Original ANDA
Division copy
Field copy

Endorsements:
HFD-620/A. High: 3/28/01 4/3/01
HFD-617/P. BeersBlock: 3/29/01 4/2/01

F/T by cll/3/30/01
V:\firmsam\bedford\ltrs&rev\72323S5.ap.doc

SUPPLEMENT APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 074531Orig1s001

MICROBIOLOGY REVIEW

OFFICE OF GENERIC DRUGS, HFD 620-640

Microbiologists Review #1

March 26, 2001

Addendum:

ANDA(s):		
	72-323/SS-005	74-531/SS-001
	72-324/SS-005	74-811/SS-002
	74-815/SS-004	75-305/SS-002
	63-313/SS-003	75-513/SS-001
	63-315/SS-002	75-524/SS-003
	74-900/SS-002	75-222/SS-001
	74-901/SS-002	75-228/SS-001
	74-441/SS-009	75-303/SS-001
	75-045/SS-002	40-347/SS-001
	75-046/SS-002	74-728/SS-002
	40-273/SS-001	89-340/SS-021
	75-405/SS-003	89-341/SS-021
	65-004/SS-002	89-342/SS-021
	74-277/SS-012	89-343/SS-021
	62-975/SS-011	74-939/SS-001
	75-634/SS-001	75-792/SS-001
	74-290/SS-010	75-421/SS-001
	74-593/SS-002	75-247/SS-001
	74-617/SS-010	81-066/SS-002

Supplements Dated:
March 6, 2001 **(Received March 7, 2001)**

Subject(s) of this Review

Conclusions: The above ANDAs are inclusive of the following NDAs Review and found **acceptable** by P Stinavich in HFD-805. The conclusion was initialed by P. Cooney. The same data applies to the above ANDAs.

Andrea S High 3/26/01

Andrea S. High, Ph. D.

cc: Original **ANDA**
Duplicate ANDA
Division Copy
Field Copy
Drafted by A. High, HFD 600 V:\microrev\72323/ss005
Initialed M. Fanning

REVIEW FOR HFD-150
OFFICE OF NEW DRUG CHEMISTRY
MICROBIOLOGY STAFF
MICROBIOLOGIST'S REVIEW #2 OF CBE-30 SUPPLEMENT
15 February 2001

A. 1. NDA 50-731/SCS-002 BC CBE-30
APPLICANT: Bedford Laboratories
300 Northfield Road
Bedford, OH 44146

2. PRODUCT NAMES: Danorubicin HCl Injection

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:
The product is intended for intravenous administration.

4. METHODS OF STERILIZATION:
The product is [redacted] (b) (4)

5. PHARMACOLOGICAL CATEGORY and/or PRINCIPLE INDICATION:
The product is to be used in combination with other anticancer drugs for remission induction in acute nonlymphocytic leukemia (myelogenous, monocytic, erythroid) of adults and for remission induction in acute lymphocytic leukemia of children and adults.

B. 1. DATE OF INITIAL SUBMISSION: 9 November 2000

2. DATE OF AMENDMENT: 25 January 2001 (Subject of this Review)

3. RELATED DOCUMENTS: DMF [redacted] (b) (4), DMF [redacted] (b) (4), AADA [redacted] (b) (4)

4. ASSIGNED FOR REVIEW: 9 February 2001

C. REMARKS: The original submission was inappropriately filed as a Changes Being Effected in 30 Days. The document should have been filed as a Prior Approval Supplement. It seeks approval of a new filling line (South Complex Facility Upgrade [redacted] (b) (4) [redacted] (b) (4) designated as Filling Line [redacted] (b) (4).

The submission seeks to provide an alternate filling line for product manufacture. The filling line is designated Filling Line [redacted] (b) (4)

and is a new line installed at the applicant's facility in a refurbished area. The area includes BVL (b) (4) (b) (4) (b) (4) The filling line is a (b) (4) filling line that is identical to the existing (b) (4) filling line at the facility. During the period from 17 October 2000 to 24 October 2000 Cincinnati District Investigator Frederick Lochner conducted an inspection. A copy of the inspection report is provided in the submission.

This submission is a response to deficiencies enumerated in Microbiologist's Review #1 dated 16 January 2001.

D. CONCLUSIONS: The application is recommended for approval on the basis of sterility assurance.

15 February 2001

Paul Stinavage, Ph.D.

PHC 2/16/01

cc: Original NDA 50-731/SCS-002
HFD-150/Div. File/D. Spillman/J. Jee/E. Duffy
HFD-805/Consult File/Stinavage

Drafted by: P. Stinavage, 15 February 2001
R/D initialed by P. Cooney

Following this page, 7 pages withheld in full (b)(4)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 074531Orig1s001

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

BEDFORD LABORATORIES™

March 6, 2001

Special Supplement - Changes Being Effected

Mr. Gary Buehler
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 NO. 74-531 REF NO. SS-001
NDA SUPPL FOR Stability PAI

RE: Special Supplement - Changes Being Effected
Product: Global Supplement

Dear Mr. Buehler,

In accordance with 21 CFR 314.70(c)(2)(C), this Special Supplement - Changes Being Effected, is being filed to provide an additional filling line for the production of [(b) (4)] products, as discussed on March 1, 2001, between Dr. Vilayat Sayeed, Deputy Directory, and Mr. Shahid Ahmed of Ben Venue Laboratories. Located in Attachment I is the corresponding FDA Form 356h.

Ben Venue Laboratories, Inc., has upgraded the South Complex to include [(b) (4)] which houses a [(b) (4)] and [(b) (4)] Filling Line. The [(b) (4)] Filling Line is identical to Ben Venue Laboratories' existing [(b) (4)] Filling Line.

Please note, Cincinnati District Investigator Frederick Lochner conducted an inspection of the [(b) (4)] from October 17, 2000 to October 24, 2000; an FD-483 was issued with a commitment from BVL to have all items to be corrected within 30 days of issuance. A copy of the Cincinnati District Inspector's report as well as BVL's response is included in Attachment II of this supplement.

Pursuant to this PAI, Bedford Laboratories™ submitted a Supplement - Changes Being Effected in 30 Days to NDA 50-731 for Daunorubicin Hydrochloride Injection, on November 9, 2000; a response to a microbiological deficiency letter was provided to the Division of Oncology Drug Products on January 25, 2001. Copies of both of these correspondences are located in Attachment III. This supplement was subsequently approved on March 5, 2001. A copy of this letter is located in Attachment IV.

A listing of the affected ANDAs follows:

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

BEDFORD LABORATORIES™

ANDAs	Products
72-323	Acetylcysteine Injection, 10%; 10 mL and 30 mL vials
72-324	Acetylcysteine Injection, 20%; 10 mL and 30 mL vials
74-815	Alprostadil Injection, USP; 0.5 mg/mL, 1 mL vials
63-313	Amikacin Sulfate Injection, USP; 50 mg/mL, 2 mL vials
63-315	Amikacin Sulfate Injection, USP; 250 mg/mL, 2 mL and 4 mL vials
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74-901	Atracurium Besylate Injection, Preserved; 10 mg/mL, 10 mL vials
74-441	Bumetanide Injection, USP; 0.25 mg/mL, 2 mL, 4 mL and 10 ml vials
75-045	Butorphanol Tartrate Injection, USP; 1 mg/mL, 1 mL vial; 2 mg/mL, 1 mL and 2 mL vials
75-046	Butorphanol Tartrate Injection, USP; 2 mg/mL, 10 mL vials
40-273	Chloroprocaine Hydrochloride Injection, USP; 20 mg/mL, 20 mL vials and 30 mg/mL, 20 mL vials
75-405	Cladribine Injection; 1 mg/mL, 8 mL and 10 mL vials
65-004	Cyclosporine Injection, USP; 50 mg/mL, 5 mL vials
74-617	Diltiazem Hydrochloride Injection; 5 mg/mL, 5 mL, 10 mL and 25 mL vials
74-939	Dipyridamole Injection; 5 mg/mL, 2 mL and 10 mL vials
74-277	Dobutamine Injection, USP; 12.5 mg/mL, 20 mL vials
62-975	Doxorubicin Hydrochloride Injection, USP; 2 mg/mL, 5 mL, 10 mL and 25 mL vials
75-634	Enalaprilat Injection; 1.25 mg/mL, 1mL and 2 mL vials
74-593	Etomidate Injection; 2 mg/mL, 10 mL and 20 mL vials
74-290	Etoposide Injection; 20 mg/mL, 5 mL, 25 mL and 50 mL vials
75-622	Famotidine Injection; 10 mg/mL, 2 mL vials (tentatively approved)
75-684	Famotidine Injection; 10 mg/mL, 50 mL vials (tentatively approved)
75-825	Famotidine Injection; 10 mg/mL, 50 mL vials (tentatively approved)
74-531	Fluphenazine Decanoate Injection, USP; 25 mg/mL, 5 mL vials
81-066	Folic Acid Injection, USP; 5 mg/mL, 10 mL
74-811	Haloperidol Decanoate Injection, USP; 50 mg/mL, 1 mL and 5 mL vials
75-305	Haloperidol Decanoate Injection, USP; 100 mg/mL, 1 mL and 5 mL vials
75-513	Inamrinone Injection; 5 mg/mL, 20 mL vials
74-524	Ketamine Hydrochloride Injection, USP; 50 mg/mL, 10 mL vials and 100 mg/mL, 5 mL vials
75-222	Ketorolac Tromethamine Injection, USP; 15 mg/mL, 1 mL vials and 30 mg/mL, 1 mL and 2 mL vials
75-228	Ketorolac Tromethamine Injection, USP; 30 mg/mL, 30 mL vials
75-303	Labetalol Hydrochloride Injection, USP; 5 mg/mL, 20 mL and 40 mL vials
40-347	Leucovorin Calcium Injection; 10 mg/mL, 30 mL and 50 mL vials
74-728	Leuprolide Acetate Injection; 1 mg/mL, 0.2 mL vials
89-340, -341, -342, 343	Methotrexate Injection, USP; 25 mg/mL, 2 mL, 4 mL, 8 mL and 10 mL vials
75-247	Midazolam Hydrochloride Injection; 1 mg/mL, 2 mL, 5 mL, 10 mL vials 5 mg/mL, 1 mL, 2 mL, 5 mL and 10 mL vials
75-792	Propranolol Hydrochloride Injection, USP; 1 mg/mL, 1 mL vials

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

BEDFORD LABORATORIES™

We trust this meets with your approval. If you have any questions or comments, please contact the undersigned at (440) 201-3333.

Sincerely,
for Bedford Laboratories™

Laurel Benzo for

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