CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40347

ADMINISTRATIVE DOCUMENTS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-347 **Date of Submission: November 19, 1998**

Applicant's Name: Bedford Laboratories

Established Name: Leucovorin Calcium Injection USP, 10 mg (base)/mL, 30 mL and 50 mL

Labeling Deficiencies:

1. GENERAL COMMENTS:

2. CONTAINER (30 mL and 50 mL)

   a. Increase the prominence of "Injection USP" to be equal to "Leucovorin Calcium" in the established name.

   b. Revise your net statements of quantity to read as follows:

300 mg*/mL (10 mg/mL)	500 mg*/mL (10 mg/mL)

3. CARTON (1 x 30 mL and 1 x 50 mL)

   a. Increase the prominence of "Injection USP" to be equal to "Leucovorin Calcium" in the established name.

   b. Revise your storage statement to include the following:

      Retain in carton until time of use.

   c. See comment (b) under CONTAINER.

4. INSERT

a. GENERAL COMMENTS

The Orphan Drug Exclusivity held by the innovator for this drug product has expired. Please revise your insert to include this information. For your convenience we have enclosed a copy of the most recently approved labeling for Leucovorin Calcium For Injection (Immunex®; Approved July 21, 1997; Revised November 1995).

b. CLINICAL PHARMACOLOGY

i. Revise the third sentence of paragraph six of this section to read as follows:

…129 ± 12 (mg·min/L ± S.E.).

Please revise your container labels, carton labeling, and insert labeling as instructed above, and submit 12 copies of final printed container labels for each package size, along with 12 copies of final printed carton labeling for each size and 4 copies of draft insert labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/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

RECORD OF TELEPHONE CONVERSATION

Bedford received a fax deficiency for ANDA 40-347 from the Agency on 2/10/2000. Bedford sent a fax to the agency on 2/16/2000 requesting a telecon to discuss the impurity specifications for the drug substance, drug product release, and stability.

In Bedford's 2/16/00 correspondence to the Agency, they have proposed data for specifications for the drug substance. (see attached fax)

Mike Smela and Ken Furnkranz reviewed the data and Mr. Furnkranz informed the firm of the following comments;

1. The specifications indicated in the table are adequate (1% for individual knowns listed, and 2% for Total Impurities).
2. Bedford should have a specification for individual unknowns.
3. Bedford should establish a specification for (since it is known to be a degradant in the drug substance/product).

Bedford provided data for specifications for drug product release and shelf-life (see attached fax).
Mike Smela and Ken Furnkranz reviewed the data and Mr. Furnkranz informed the firm of the following comments;

1. Bedford should establish specifications for all identified impurities present in the drug substance for the drug product unless those impurities are proven (conclusively) that they are not degradants.
2. The same specifications as allowed for the Individual Known Impurities %) and Total Impurities %) in the drug substance are adequate for the drug product at release.
3. For stability, a specification of NMT % for all known impurities, and % for Total Impurities is acceptable.
4. Specifications for individual unknowns, as indicated in the 2/16/2000 correspondence (NMT % at Release and NMT % on Stability) are acceptable.

Mr. Ahmed agreed to respond to the fax amendment by 3/10/2000.

DATE
March 3, 2000

ANDA NUMBER
40-347

IND NUMBER

TELECON

INITIATED BY

X **SPONSOR**

FDA

PRODUCT NAME
Leucovorin Calcium Injection USP, 10 mg(base)/mL, 30 mL and 50 mL vials

FIRM NAME
Bedford Laboratories

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Shahid Ahmed
Molly Rapp

TELEPHONE NUMBER
(440) 232-3320
Ext# 333

SIGNATURE

K. Furnkranz
M.Dillahunt

/S/
3/3/00

/S/
3/3/00

V:\FIRMSAM\BEDFORD\TELECONS\40347.tcon1.doc
CC: ANDA 40-347
Chem Div I, T-con Notebook

ANDA 40-347

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

JAN 12 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.

Reference is made to the telephone conversation dated December 9, 1998 and your correspondence dated December 16, 1998.

NAME OF DRUG: Leucovorin Calcium Injection USP, 10 mg (base)/mL, 30 mL and 50 mL vials

DATE OF APPLICATION: November 19, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 20, 1998

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:

Denise Huie
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