

**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

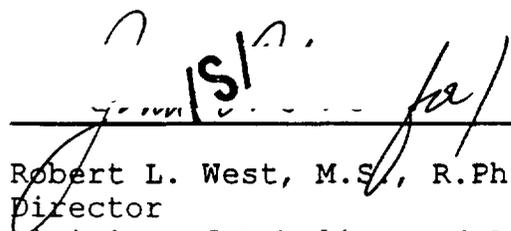
- i. Revise the third sentence of paragraph six of this section to read as follows:

...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.


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

<p>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.</p> <p>In Bedford's 2/16/00 correspondence to the Agency, they have proposed data for specifications for the drug substance. (see attached fax)</p> <p>Mike Smela and Ken Furnkranz reviewed the data and Mr. Furnkranz informed the firm of the following comments;</p> <ol style="list-style-type: none"> 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). <p>Bedford provided data for specifications for drug product release and shelf-life (see attached fax).</p> <p>Mike Smela and Ken Furnkranz reviewed the data and Mr. Furnkranz informed the firm of the following comments;</p> <ol style="list-style-type: none"> 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. <p>Mr. Ahmed agreed to respond to the fax amendment by 3/10/2000.</p>	<p>DATE March 3, 2000</p>
	<p>ANDA NUMBER 40-347</p>
	<p>IND NUMBER</p>
	<p align="center">TELECON</p>
	<p>INITIATED BY</p>
	<p>X SPONSOR</p>
	<p align="center">FDA</p>
	<p>PRODUCT NAME Leucovorin Calcium Injection USP, 10 mg(base)/mL, 30 mL and 50 mL vials</p>
	<p>FIRM NAME Bedford Laboratories</p>
	<p>NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD Shahid Ahmed Molly Rapp</p>
<p>TELEPHONE NUMBER (440) 232-3320 Ext# 333</p>	
<p>SIGNATURE</p> <p>K. Furnkranz M. Dillahunt</p> <p align="right">   </p>	

3/3/00
J

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CC: ANDA 40-347

Chem Div I, T-con Notebook

