DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 8-107/S-051

JUL 21 1997

Immunex Corporation
51 University Street
Seattle, Washington 98101

Attention: Susan C. Sullivan
Manager, Regulatory Affairs

Dear Ms. Sullivan:

Please refer to your October 2, 1996 supplemental new drug application (S-051) received October 3, 1996 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Leucovorin Calcium for Injection.

The supplemental application (S-051), Special Supplement - Changes Being Effected, provides an additional statement in the WARNINGS section (with its corresponding reference in the REFERENCES section) as follows:

> Seizures and/or syncope have been reported rarely in cancer patients receiving Leucovorin, usually in association with fluoropyrimidine administration, and most commonly in those with CNS metastases or other predisposing factors, however, a causal relationship has not been established.[5]
>
> 5. Meropol NJ, Creaven PJ, White RM, et al, "Seizures Associated With Leucovorin Administration in Cancer Patients." J NCI 1995;87(1):56-58.

In addition, we acknowledge inclusion within this supplemental application minor changes in the package insert, container and carton labeling which are in accordance with 21 CFR 314.70 (d) Changes described in the annual report.

We have completed the review of this supplemental application with final printed labeling (package insert, carton and immediate container) and it is approved effective on the date of this letter. However, we request that you further revise your labeling to include the following changes within 6 months or at the next printing, whichever occurs sooner.

1. In the HOW SUPPLIED section in the package insert and on the carton labeling, revise the storage statement to read:

   Store at 25°C (77°F); (b) (4) (59- (b) (4) °F)

2. Revise the storage statement on the immediate container. Where space on the

immediate container is limited and an abbreviated labeling statement is necessary, either of the following statements may be appropriate.

Store at 25°C (77°F) [redacted] (59- [redacted]°F)

or

Store at 25°C (77°F)

Please note that this supplemental application (S-051), does not include revisions requested in our approval letter for S-050 dated May 24, 1996. In addition, it is the current policy for oncology drug labeling to include only references pertaining to safe handling of oncologic drugs. All other references should be deleted from the package insert.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact Leslie Vaccari, Project Manager, (301) 594-5778.

Sincerely yours,

Robert J DeLap 20 JULY 1997

Robert J. DeLap, M.D., Ph.D.
Director
Division of Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 8-107
HFD-150/Div. files
HFD-150/LVaccari
HFD-101/L.Carter
DISTRICT OFFICE
HF-2/Medwatch (with labeling)
HFD-80 (with labeling)
HFD-613 (with labeling)
HFD-735/(with labeling)

Drafted by: LVaccari/3-14-97/FT 7-18-97

R/D init. By: DPease/3-17-97
RWhite/3-18-97
JJohnson/3-18-97
DKlein/7-14-97
ETolgyesi/7-15-97

final: D Good 7-18-97

SUPPLEMENT APPROVAL (S-051 with FPL)