CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

STN 103795/5102

Biores research Monitoring
MEMORANDUM

DATE MAY 23 2003

FROM Christine Drabick, Bioresearch Monitoring Branch, HFM-664
Division of Inspections and Surveillance
Office of Compliance and Biologics Quality

TO Elektra Papadopoulos, HFM-582
Chair, BLA Committee
Karen Jones, HFM-588

SUBJECT Bioresearch Monitoring Inspection Results
BLA: STN 103795/5102
Product: Enbrel®
Sponsor: Immunex Corporation

SUMMARY STATEMENT

The results of bioresearch monitoring inspections of three clinical sites indicate that the submitted data can be considered reliable and accurate with exceptions noted.

BACKGROUND

Inspections of three clinical investigators were performed in support of the subject Biologics License Application (BLA) Supplement. 205 subjects were enrolled in the study at seventeen study centers in the United States. Subject population and geographic distribution determined the site selections. The total subject population at the three inspection sites was 43 (21%). Copies of information from the BLA were compared with source documents during the inspection. The inspections focused on specific questions concerning the study identified below.

STUDY TITLE:

Double-blind, Randomized, Placebo-controlled Phase 3 Study of Enbrel® in the Treatment of Psoriatic Arthritis (PsA) and Psoriasis: Radiographic Results

Study Dates: 3/31/00 to 8/8/02 205 subjects
INSPECTIONAL FINDINGS

1. Failure to ensure that the investigation is conducted according to the signed investigational plan. [21 CFR § 312.60].

The following deviations occurred at Dr. Cohen’s site:

A. Subject 0076 was enrolled in the study while continuing to receive a weekly dose of 30 mg methotrexate, although Section 4.1 of the protocol specifies that enrolled subjects on concomitant methotrexate should receive weekly doses of 25 mg or less.

B. The following periodic assessments were not completed as required by the protocol:
   i. Week 36 evaluations for Subject 0606, Week 24 evaluations for Subjects 041 and 0064, and Week 12 evaluations for Subject 056.
   ii. Week 24 evaluations scheduled on 11/30/00 for subject 0048 were performed on _ because the subject failed to appear for the _ appointment.

C. Subject clinical visits were not conducted within five days of the stipulated time point for evaluation as required by Section 7.0 the protocol.
   i. Subject 0046 was scheduled for a Week 12 clinical visit on _ but was not evaluated until _
   ii. Subject 0076 was scheduled for a Week 12 clinical visit on _ but was not evaluated until _
If you have any questions or comments about the contents of this memo or any aspect of Bioresarch Monitoring, please contact me at (301) 827-6323.

窳

Christine Drabick
Consumer Safety Officer

Attachments: Form FDA 483s for Drs. Cohen and Gottlieb
Application Number 103795/5102

Letter Type: BIMO Summary

cc:

**Hard Copy**
HFM-99    IND  #8806
HFM-600
HFM-664  Access/Chron
HFM-664  Drabick
HFM-664  BLA Summary File

**Scanned Electronic Copy**
HFM-582    Siegel
HFM-582    Papadopoulos, Chair STN103795/5102
HFM-588    Jones
HFM-573    Mills
HFM-219    Misra
HFM-650    Cole

HFR-SW100  Michael Chappell, Director
HFR-SW1540  Joel Martinez, BIMO Coordinator
HFR-SW150  Christopher Rush, Investigator
HFR-SW150  Scott Nichols, Investigator

HFR-CE700  Joann Givens, Director
HFR-CE250  Nancy Bellamy, BIMO Coordinator
HFR-CE2565  William Tingley, Investigator

HFR-CE300  Douglas Ellsworth, Director
HFR-CE3565  Shirley Isbill, BIMO Coordinator
HFR-CE350  Byungja Marciante, Investigator