



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

40088d

Center for Biologics Evaluation and
Research
1401 Rockville Pike
Rockville MD 20852-1448

By Certified Mail – Return Receipt Requested
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CBER -07-001

Warning Letter

OCT 12 2006

David A. Lein, M.D.
6032 McGee
Kansas City, Missouri 64113

Dear Dr. Lein:

This letter describes the results of a Food and Drug Administration (FDA) inspection that was conducted from June 7 through June 12, 2006. FDA investigator Carl Montgomery met with staff at the Kansas City Free Health Clinic to review the conduct of a clinical study entitled [REDACTED]

[REDACTED] for which you were principal investigator. FDA conducted this inspection under the agency's Bioresearch Monitoring Program, which includes inspections designed to review the conduct of research involving investigational devices.

At the end of the inspection, a Form FDA 483, Inspectional Observations, was issued and discussed with Sheridan Wood, Executive Director of the Kansas City Free Health Clinic. We reviewed her letter dated June 12, 2006, responding to the Form FDA 483.

We have determined that you violated regulations governing the proper conduct of clinical studies involving investigational devices, as published in Title 21, Code of Federal Regulations (CFR), Part 812 (available at <http://www.gpoaccess.gov/cfr/index.html>). The applicable provisions of the CFR are cited for each violation listed below.

1. **You failed to fulfill the responsibilities of an investigator [21 CFR § 812.100 and 21 CFR § 812.110(b)].**

An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan, and all applicable regulations for protecting the rights, safety, and welfare of subjects under the investigator's care, and for the control of devices under clinical investigation.

Our investigation reveals that you failed to fulfill your responsibilities as a clinical investigator under 21 CFR 812.100 and 21 CFR 812.110(b) in that you failed to maintain an adequate internal quality control program and to immediately

document and report all protocol deviations, as required by the protocol. More specifically, on several occasions, your staff falsified study subject consent forms, which falsifications you have admitted the existence of in a letter dated January 20, 2004, to the President of [REDACTED] ("letter to [REDACTED]").

Examples of some of the falsifications are as follows:

- The consent forms for subjects [REDACTED] were apparently filled out by a clinic staff member who signed as both the study subject and as the staff member administering the consent, as you explained in your letter to [REDACTED]
- The consent forms for study subjects [REDACTED] and [REDACTED] were apparently filled out by a staff member who signed as a study subject using false names, as you explained in your letter to [REDACTED] and [REDACTED]
- One study subject was apparently enrolled three times under the same name but under different study subject numbers ([REDACTED] on 6/10/03, [REDACTED] on 8/28/03, and [REDACTED] on 11/04/03), as you explained in your letter to [REDACTED]

2. You failed to maintain accurate, complete, and current records relating to your participation in the investigation, and you failed to prepare and submit complete, accurate, and timely reports to the sponsor [21 CFR §§ 812.140 and 812.150].

- A. An investigator is required to maintain accurate, complete and current records relating to their participation in the investigation. This requirement includes a need to maintain accurate, complete and current records regarding the names of all persons who received, used or disposed of each device (21 CFR 812.140(a)(2)), accurate, complete and current records of each subject's case history, including consent forms, and details of the exposure to the device (21 CFR 812.140(a)(3)), and accurate, complete and current records of all instances of deviation from the protocol, together with dates of, and reasons for, such deviations (21 CFR 812.140(a)(4)).

Our investigation reveals that you did not maintain accurate, complete and current records relating to your participation in the investigation, more specifically, that the records you maintained relating to the individuals detailed in the table below are false (including the names of subjects who received the devices, their case histories, consent forms, details of their exposure to the device, and the records of any instances of deviation from the protocol), as you have admitted in your letter to [REDACTED]

- B. An investigator is required to submit complete, accurate and timely progress reports on the investigation to the sponsor, the monitor and the reviewing IRB at regular intervals (21 CFR 812.150(a) (3)), and is also required to submit a complete, accurate and timely final report to the sponsor and the reviewing IRB within 3 months after termination or completion of the investigation (21 CFR 812.150(a) (5)).

Our investigation reveals that the reports that you submitted to the sponsor and the reviewing IRB relating to the individuals detailed in the table below are false (including the names of subjects who received the devices, their case histories, consent forms, details of their exposure to the device, and the records of any instances of deviation from the protocol), as you have admitted in your letter to [REDACTED]

| Subject # | Subject | Staff Administering Consent | Consent Date | CRF Signed by Dr. Lien | Whether Samples and Case Report Forms were Submitted to the Sponsor | Sample ID # |
|------------|------------|-----------------------------|--------------|------------------------|---|-------------|
| [REDACTED] | [REDACTED] | [REDACTED] | 8/28/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 6/23/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 11/05/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 6/10/03 | | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 8/28/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 11/04/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 8/28/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 11/05/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 6/10/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 8/28/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 6/10/03 | | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 11/05/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 7/07/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 7/22/03 | Yes | Yes | [REDACTED] |
| [REDACTED] | [REDACTED] | [REDACTED] | 7/17/03 | Yes | Yes | [REDACTED] |

3. **You failed to protect the rights, safety, and welfare of the subjects under your care, and you failed to ensure that the investigation was conducted according to the investigational plan and the signed agreement [21 CFR § 812.100].**

Our investigation reveals that you did not fulfill your responsibilities as a clinical investigator under 21 CFR 812.100 in that you failed to ensure that informed consent was obtained, you failed to maintain an adequate internal quality control program and to immediately document and report all protocol deviations, all as required by the protocol. More specifically, the protocol and the HIV-1 Sample Collection Case Report Form Instructions require that enrolled subjects be 18 years of age or older. However, on at least three occasions detailed in the table below, you enrolled subjects [REDACTED] and [REDACTED] in the study despite the fact that they were under the age of 18 at the time of study enrollment, all this in violation of 21 CFR 812.100.

| Subject # | Age | Date Enrolled | [REDACTED] ID # |
|------------|-----|---------------|-----------------|
| [REDACTED] | 17 | 6/11/03 | [REDACTED] |
| [REDACTED] | 17 | 6/16/03 | [REDACTED] |
| [REDACTED] | 17 | 7/07/03 | [REDACTED] |

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical studies. It is your responsibility as a clinical investigator to ensure compliance with the Act and all applicable regulations.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the clinical investigator. In addition, please provide a complete list of all clinical trials in which you have participated for the last five years, including the name of the study and test article, the name of the sponsor, the number of subjects enrolled, and the current status of the study. Failure to respond to this letter and to take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. In addition, FDA could initiate disqualification proceedings against you in accordance with 21 C.F.R. 812.119.

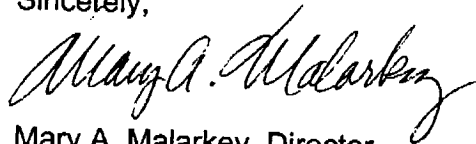
Page 5 -- Dr. Lein

Please send your written response to:

Solomon Yimam
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
Food and Drug Administration
1401 Rockville Pike, Suite 200N
Rockville, Maryland, 20852-1448
Telephone: (301) 827-1948

We also request that you send a copy of your response to the FDA office listed below.

Sincerely,



Mary A. Malarkey, Director
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

cc: Sheridan Y. Wood
Executive Director
Kansas City Free Health Clinic
3515 Broadway
Kansas City, Missouri 64111

John Thorsky, Director
Kansas City District Office
Food and Drug Administration
11630 West 80th Street
Lenexa, Kansas 66214 -3340