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

July 19, 2000

**WARNING LETTER**

CBER-00-027

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

David W. Andrews, M.D.  
Associate Professor and Attending Physician of Neurosurgery  
Thomas Jefferson University Hospital  
Walnut Towers, Suite 650  
834 Walnut Street  
Philadelphia, Pennsylvania 19107

Dear Dr. Andrews:

During the inspection ending on May 31, 2000, Ronald Stokes, an investigator with the Food and Drug Administration (FDA), reviewed your conduct of the study

\_\_\_\_\_ This inspection was conducted under the FDA's  
Bioresearch Monitoring Program which includes inspections designed to monitor the  
conduct of clinical research involving investigational drugs.

At the close of the inspection, a Form FDA 483 (Attachment A) was issued. This inspection revealed deviations from applicable federal regulations as published in Title 21, Code of Federal Regulations, Part 312. [21 CFR 312] These deviations include, but are not limited to, the following items:

**1. Failure to insure that the investigation was conducted according to the signed investigational plan (protocol). [21 CFR 312.60]**

You gave an investigational product that should have been \_\_\_\_\_ as required by a Standard Operating Procedure (SOP) of the sponsor \_\_\_\_\_ to two subjects \_\_\_\_\_

SOP 131.1, entitled \_\_\_\_\_  
\_\_\_\_\_ says \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

**2. Failure to maintain adequate and accurate case histories, including signed and dated consent forms. [21CFR 312.62 (b)]**

- a. You did not have signed consent forms for three subjects \_\_\_\_\_ enrolled in the study.
- b. The consent form for the fourth subject \_\_\_\_\_ was signed by the \_\_\_\_\_, without documentation as to why the subject did not sign their own form. According to the Case Report Forms for this subject, the Karnofsky score was \_\_\_\_\_ and the inclusion criterion of the ability of the subject to give informed consent was satisfied.

**3. Failure to report serious adverse events to the Institutional Review Board (IRB) within the time frame required by the IRB. [21 CFR 312.66]**

You did not report adverse events experienced by subject \_\_\_\_\_ until several months after occurrence. Your IRB required that any serious and/or unexpected adverse reactions be reported to the IRB within \_\_\_\_\_. There was a delay of several months before these adverse events were reported. In addition, the adverse event report forms were incomplete. The question, "In your opinion, was the event caused by the therapy or procedures associated with this protocol?" was not answered, and the line for "Signature of Principal Investigator" was blank.

Your signature on Form FDA 1572, Statement of Investigator, indicates your agreement to comply with all requirements regarding the obligations for clinical investigators conducting human clinical trials and all other pertinent requirements in 21 CFR 312. It is your responsibility to ensure adherence to each requirement of the law and applicable regulations.

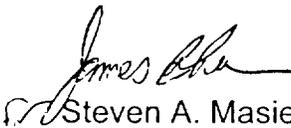
Please notify this office in writing, within 15 business days of the receipt of this letter, of the steps you have taken to correct the noted violations, as well as any steps taken to prevent the occurrence of similar violations in ongoing and future studies. If corrective action cannot be completed within 15 business days, please state the reason for the delay and the time within which the corrections will be completed.

Failure to achieve correction may result in enforcement action without further notice. These actions could include initiation of investigator disqualification procedures, which may render a clinical investigator ineligible to receive investigational new drugs, and the termination of an investigational new drug application (IND).

Please send your written response to:

Mary Andrich, M.D.  
Office of Compliance and Biologics Quality, HFM-664  
Center for Biologics Evaluation and Research  
Food and Drug Administration  
1401 Rockville Pike  
Rockville, Maryland, 20852

Sincerely,

  
Steven A. Masiello

Director  
Office of Compliance and Biologics Quality  
Center for Biologics Evaluation and Research

Attachments:

Attachment A: Form FDA 483, Inspectional Observations, dated May 23, 2000.

cc:

J. Bruce Smith, M.D.  
Chairman, Institutional Review Board  
Jefferson Medical College of Thomas Jefferson University  
1020 Locust Street  
Room M-5  
Philadelphia, Pennsylvania 19107

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