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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEDERAL EXPRESS

JUN 24 1997

WARNING LETTER

Kenneth R. Davis, M.D.
Department of Neuroradiology
Massachusetts General Hospital
32 Fruit Street
Boston, Massachusetts 02114

Dear Dr. Davis:

You were inspected between February 27 and March 27, 1997, by Paraluman S. Leonin and John A. Hamilton III, investigators with the Food and Drug Administration (FDA), Boston District Office. The purpose of that inspection was to determine whether your activities as a sponsor/investigator for the investigational study of the [redacted] complied with applicable FDA regulations. This product is considered a device as that term is defined in section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act).

Our review of the inspection report submitted by the District Office revealed violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions. These items were observations on a Form FDA-483 which was presented to and discussed with you at the conclusion of the inspection. The following list of violations is not intended to be an all-inclusive list of deficiencies in the above referenced clinical study:

1) **Failure to conduct an investigation in accordance with the conditions of approval imposed by the Institutional Review Board (IRB) as required by 812.110(b).**

   The Subcommittee on Human Subjects (SHS), your IRB, requires that a written report of the death of any research subject be made within 5 business days. The review of records of your study disclosed that since 1987, five or more subject deaths have not been reported to the IRB.

2) **Failure to ensure that proper informed consent is obtained as required by 21 CFR 812.100.**

   The informed consent documents were not signed for five subjects. 21 CFR 50.27 requires that a written consent form be signed by the subject or the subject's legally authorized representative.

3) **Failure to maintain accurate, complete and current records relating to receipt, distribution and use of the study devices as required by 21 CFR 812.140(a).**

There was lack of inventory control of devices in that records documenting the names of all persons who received, used or disposed of each device were incomplete. While your November 9, 1996, letter to FDA indicated that 109 subjects were treated with investigational devices, study records provided accurate accounting of devices for only twelve subjects.

4) **Failure to maintain records relating to investigator agreements as required by 21 CFR 812.140(b).**

As sponsor of this device study you are required to obtain signed investigator agreements from each co-investigator prior to their treatment of any subjects with study article. Signed agreements were not available for four of six participating investigators.

5) **Failure to submit complete, accurate and timely reports of the progress of the investigation to the IRB and FDA as required by 21 CFR 812.150(b)(5).**

Between September 22, 1992 and October 29, 1996, you did not accurately report on the progress of your investigation.

A letter from FDA to you, dated January 31, 1992, reminded you of your responsibilities as a sponsor of a significant risk device investigation which includes the requirement to submit a progress report to FDA on at least a yearly basis. You failed to do this for the period above (1992-1996).

6) **Failure to monitor the investigation and to secure the compliance of your study co-investigators as required by 21 CFR 812.46.**

Between 1992 and 1996, two co-investigators did not report study subjects deaths to the institutional review board (IRB) on a timely basis. Inadequate monitoring of the investigation resulted in your failing to secure compliance with the conditions of IRB approval.

The above description of deviations is not intended to be an all-inclusive list of deficiencies in your clinical study. It is your responsibility to ensure adherence to all requirements of the Act and regulations relevant to device clinical investigations.

We acknowledge your April 20, 1997, response addressing the inspectional observations. In this letter you deny any responsibility for the violations and you reference previous correspondence with FDA. Our review of these letters, wherein you disclose your lack of adequate monitoring and reporting, leads us to conclude that the study is no longer under your control. For this reason, we are apprising the Office of Device Evaluation of our conclusions regarding the documented monitoring and reporting problems associated with this Investigational Device Exemption (IDE).

If you should wish to make a response, or you have questions concerning this matter, send them to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch I (HFZ-311), 2098 Gaither Road, Rockville, Maryland 20850, Attention: L. Glenn Massimilla, R.Ph., telephone (301) 594-4720, ext. 136.

Sincerely yours,

for Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health