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Via Federal Express

JAN 28 2002

Food and Drug Administration  
2098 Gaither Road  
Rockville MD 20850

**WARNING LETTER**

Mark S. Allen, M.D.  
Mayo Clinic  
112 7<sup>th</sup> Street NE  
Rochester, Minnesota 55906

Dear Dr. Allen:

This Warning Letter informs you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site and requests from you a prompt reply informing us of your corrective actions. You participated as a clinical investigator in a study entitled, [REDACTED]

[REDACTED] to investigate the device [REDACTED]. Data from the study conducted at your site was submitted to the FDA in support of the premarket approval application [REDACTED].

During the period of November 14 through December 6, 2001, you were visited by William E. Keer, an investigator from the FDA's Minneapolis District Office. The purpose of Mr. Keer's visit was to conduct an inspection to determine whether your activities and procedures as a clinical investigator for the [REDACTED] study complied with applicable regulations. This product is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

This inspection was conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approval (PMA), and Premarket Notification (510(k)) submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

We have completed our review of the inspection report submitted by the Minneapolis District Office. The report reveals significant violations of the requirements under Title 21, Code of Federal Regulations (21 CFR), Part 50 - Protection of Human Subjects; 21 CFR Part 56 - Institutional Review Boards; and 21 CFR Part 812 - Investigational Device Exemptions. These violations are listed on the Form FDA 483 "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. The violations noted on the Form FDA 483 and our subsequent review of the inspection report are summarized below:

**Failure to prepare and submit complete, accurate, and timely reports (21 CFR § 812.150 (a)(1)).**

You failed to prepare and submit to the institutional review board timely reports. For example, two study subjects died [REDACTED] and [REDACTED] and one study subject [REDACTED] was hospitalized for renal failure. These unanticipated adverse device effects were not submitted to the institutional review board in a report as soon as possible and within 10 working days after first learning of the effect.

**Failure to obtain legally effective informed consent from study subjects (21 CFR Part 50 and 21 CFR § 812.100).**

You failed to ensure that legally effective informed consent was obtained. For example, study subjects with randomization numbers [REDACTED] through [REDACTED] signed a wrong version of the consent form.

**Failure to maintain accurate, complete, and current records relating to the investigation (21 CFR §812.140(a)).**

- You failed to maintain documents evidencing informed consent. For example, original informed consent forms for study subjects [REDACTED], and [REDACTED] were lost and therefore, not found in the study records.
- You failed to record completely and accurately treatment of study subjects with concomitant medications. Missing from the concomitant medications and treatment reports were the reasons for the prescriptions, dates medications started and discontinued.
- You failed to maintain test article accountability records. For example, test article accountability documents were not complete due to missing dates received, number received, lot numbers, and subject identifications.

**Failure to control the use of devices under investigation (21 CFR §§ 812.100 and 812.110).**

You failed to control the use of devices under investigation and maintain test article accountability. For example, the document *Investigator Accountability/Disposition Record* was not maintained. Some time after August 13, 2000 the form was not kept current. The blocks for date received, number received, lot number and subject identification were left blank from September 5 to October 13, 2000.

The violations listed above are not intended to be an all-inclusive list of deficiencies at your site. As a clinical investigator, it is your responsibility to ensure that investigations that you participate in are conducted in accordance with applicable FDA regulations. To assist you, we have enclosed a copy of the *FDA Information Sheets*, guidance for clinical investigators.

Please advise this office, in writing, within fifteen working days of receipt of this letter, of the specific steps that you have taken to correct these violations and other violations known to you, and to prevent the recurrence of similar violations in current or future studies. Failure to respond may result in regulatory action, including disqualification, without further notice.

You should direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch II (HFZ-312), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Viola Sellman, Branch Chief.

A copy of this letter has been sent to our Minneapolis District Office, 240 Hennepin Avenue, Minneapolis, Minnesota 55401. We request that a copy of your response be sent to that office as well.

Sincerely yours,



Larry Spears  
Acting Director  
Office of Compliance  
Center for Devices and  
Radiological Health

Enclosure

cc:

