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Via Federal Express

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

MAR 24 2000

James F. Jekel, M.D., M.P.H.
Chairman
Institutional Review Board
Griffin Hospital
130 Division Street
Derby, Connecticut 06418

Dear Dr. Jekel:

During the period of February 9-15, 2000, Mr. George Allen, an investigator from the Food and Drug Administration's (FDA) New England District Office visited the Institutional Review Board (IRB) at your facility. The purpose of this visit was to determine whether the IRB's procedures complied with the requirements of Title 21, Code of Federal Regulations (21 CFR), Part 56 - Institutional Review Boards, Part 50 - Protection of Human Subjects and Part 812 - Investigational Device Exemptions. These regulations apply to clinical studies of products regulated by the FDA.

Serious deviations from the requirements were noted during the inspection. These deviations were listed on the Form FDA 483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. Some of the deviations noted remain uncorrected from a 1987 inspection. Also present was [REDACTED] IRB Coordinator. Our review of the inspection report revealed the following deficiencies:

The IRB's standard operating procedures do not cover all the required functions and operations of an IRB as required under 21 CFR 56.108. For example:

- The IRB lacks written procedures for conducting initial and continuing review of research. There was no documentation that IRB members received copies of protocols and consent forms to review prior to IRB meetings. There was no documentation that at least one IRB member was assigned the responsibility to do an in-depth evaluation of the protocol and consent form prior to the review and approval of the study.
- There are no written procedures to document how alternate members are selected, to describe their duties and responsibilities, whom they are to replace, and to ensure that they receive the same information as the primary member.

- The IRB does not have written procedures for distinguishing between significant risk (SR) and non-significant risk (NSR) device studies. This determination should be done during the initial review of studies in accordance with 21 CFR 812.66.
- There are no written procedures for handling of expedited reviews. Expedited review procedures are required by 56.110 for certain kinds of research involving no more than minimal risk, and for minor changes in approved research. There are also no written procedures to follow for emergency use.

Meeting minutes are deficient in that:

- Minutes for five of nine meetings reviewed for the past two years do not indicate the members voting for, against, or abstaining from a proposal as required by the IRB's written procedures and 21 CFR 56.115(a)(2). **This deficiency was also noted during a 1987 inspection and remains uncorrected.**
- Members attending meetings during the past two years were not identified as to their affiliation with the IRB. Their names did not appear on the IRB's membership list of primary and alternate members.
- There were no records maintained to document that the IRB's request for changes or conditions of approval were followed up by the IRB. **This deficiency was also noted during a 1987 inspection and remains uncorrected.**
- The actual SR/NSR determination for the [REDACTED] was not recorded in the minutes of the IRB meeting.

The deviations listed above are not intended to be an all-inclusive list of deficiencies. The IRB is responsible for adhering to each requirement of the law and relevant regulations.

We are enclosing a copy of the FDA Information Sheets for Institutional Review Boards and Clinical Investigators for your information and to assist you in revising your IRB's written operating procedures. Appendix H, entitled "A Self-evaluation Checklist for IRBs," of the enclosure, provides additional information to assist you.

For further information concerning the Bioresearch Monitoring Program, please visit our Internet homepage at <http://www.fda.gov/cdrh/comp/bimo.html>. Valuable links to related information are included at this site.

Within fifteen (15) working days of receipt of this letter, please provide this office with written documentation of any specific steps you have taken or will be taking to bring your IRB into compliance with FDA regulations. The corrective actions should include revisions to the IRB's written procedures and the timeframes within which these procedures will be developed and implemented. Please be aware that your corrective actions may be verified during a future FDA inspection.

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: Robert K. Fish, Consumer Safety Officer. A copy of this letter has been sent to our New England District Office, One Montvale Avenue, Stoneham, Massachusetts 02180. We request that a copy of your response also be sent to that office.

Please direct all questions concerning this matter to Mr. Fish at (301) 594-4723, ext. 138.

Sincerely yours,



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

Enclosure

cc: Michael Carome, M.D.
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