DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Rockville MD 20857

WARNING LETTER

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FEDERAL EXPRESS

David S. Kemler, Ph.D.
Chairman
Institutional Review Board
Southern Connecticut State University
501 Crescent Street
New Haven, Connecticut 06515

Dear Dr. Kemler:

During the period of August 17-19, 1999, Mr. Edward Janik, an investigator from the Food and Drug Administration's (FDA) New England District Office inspected the Institutional Review Board (IRB) at your facility. The purpose of that inspection was to determine whether the IRB's activities and procedures for the protection of human subjects involved in clinical studies of FDA-regulated products complied with applicable FDA regulations.

Our review of the inspection report and exhibits submitted by the district office revealed that there were deviations from 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 deviations were listed on the Form FDA 483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection. The list of violations that follows is not intended to be an all-inclusive list of IRB deficiencies.

1. **Failure to have and follow written procedures for IRB functions and operations in accordance with 21 CFR 56.108, 56.115(a)(6), and 812.66.**

   There are no written procedures that adequately describe the IRB's functions and operations. For example, the IRB lacks written procedures for conducting initial and continuing review of research and for reporting findings and actions to the IRB and/or the investigator. In order to fulfill its obligations under Part 56, an IRB is required to follow written procedures for conducting initial and continuing review of research. There was no documentation that IRB members received copies of protocols and/or informed consents 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.

We also note that the IRB lacks 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 reviewed by the IRB. You stated that IRB members have received copies of 21 CFR Part 812. However, that does not suffice for the IRB's lack of having written procedures, nor does it ensure that the IRB actually discusses the issue of SR/NSR studies during the initial review process. We also note that the Southern Connecticut State University (SCSU) IRB has no written procedures detailing how the IRB performs expedited review or emergency use review.

Each IRB that reviews clinical studies subject to 21 CFR Parts 50 and 56 of the FDA regulations must have and follow written procedures that specifically describe the IRB's functions and operations. The SCSU IRB has no formalized written procedures currently being utilized, as required by 21 CFR 56. The IRB uses the "Institutional Integrity and Ethics Document for SCSU" document for its written procedures. This document does not fulfill the requirement of having written IRB procedures. As noted in the inspection report, the IRB's procedures need to be extensively revised to accurately reflect the IRB's functions and operations.

2. **Failure to have and follow written procedures that document the IRB's authority to approve, review and/or require modifications in research activities involving human subjects in accordance with 21 CFR 56.109(a).**

   There are no written procedures that adequately describe how the IRB documents its authority to approve modifications in research activities involving human subjects. An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities.

3. **Failure to document the IRB's authority to disapprove research and that the institution cannot override the IRB's decision to disapprove research in accordance with 21 CFR 56.112.**

   There are no written procedures that adequately describe the IRB's authority to disapprove research and that its decision may be subject to further review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by the IRB.

4. **Failure to document the IRB's authority to terminate approval of research in accordance with 21 CFR 56.113.**

   The IRB has no written procedures that describe the IRB's authority to suspend or terminate approval of research that is not being conducted in accordance with IRB requirements. An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

5. **Failure to ensure that informed consent documents comply with the requirements of 21 CFR 50.25.**

   The IRB failed to ensure that the IRB approved informed consent used in the [redacted] study sponsored by [redacted] contained a confidentiality statement that FDA personnel may review or inspect the medical records of study subjects.

6. **Failure to maintain IRB records in accordance with 21 CFR 56.115(a).**

   The IRB failed to maintain records of meeting minutes. For example, minutes of meetings that were held to discuss, approve and/or modify the [redacted] protocol were not available for review by Mr. Janik. There was no documentation that the IRB reviewed and approved the initial protocol and modifications.

   An IRB is required to prepare and maintain adequate documentation of IRB activities including minutes of meetings in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on actions taken including the number of members voting for, against, or abstaining; the basis for requiring changes in or disapproval of research; and a written summary of the discussion of controverted issues and their resolution.

We note that the issue of IRB membership was also discussed with you during the inspection. At the time of the inspection, there was no documentation of IRB membership. The IRB membership list provided to Mr. Janik does not meet the requirements of 21 CFR Parts 56.107 and 56.115(a)(5). For example, the list does not identify the members' representative capacity and their areas of expertise. Furthermore, the IRB membership may not consist entirely of members of one profession. We note that six of the seven IRB members are faculty members of SCSU. The other member is listed as not being associated with the institution.

We are enclosing a copy of the FDA Information Sheets for Institutional Review Boards and Clinical Investigators for your information 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, Attn: 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 be sent to that office.

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

Sincerely yours,

Charmaine O'Connor, RPh

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

Enclosure

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