DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

SEP 27 2000

WARNING LETTER

Federal Express

Joyce Heinrich
President
Texas Applied Biotechnology Research
Review Committee
8303 Southwest Freeway
Suite 835
Houston, Texas 77074

Dear Ms. Heinrich:

During the period of April 20 through May 10, 2000, Ms. Andrea Branche and Ms. Tricia Samaniego, investigators from the Food and Drug Administration's (FDA) Dallas District Office, conducted an inspection of the Texas Applied Biotechnology Research Review Committee (IRB). The purpose of the inspection was to determine whether your procedures complied with Title 21, Code of Federal Regulations (21 CFR), Part 50 – Protection of Human Subjects, Part 56 - Institutional Review Boards, and Part 812 – Investigational Device Exemptions. These regulations apply to clinical studies of products regulated by the FDA.

Our review of the inspection report and exhibits submitted by the district office revealed serious deviations from pertinent regulations. 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 Form FDA 483 was annotated to reflect your promise to take corrective action. Deviations noted on this form are summarized below:

Failure to prepare and maintain written procedures according to 21 CFR 56.108.

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 as required by 21 CFR 56.108. The inspection report shows that the IRB's written procedures, "Guidelines for Submissions of Protocols and Investigational Device Exemption Applications," do not include procedures for:

- conducting initial and continuing review of research;
- determining which projects require review more often than annually ;
- ensuring prompt reporting to the IRB of changes in research;

- ensuring that changes in approved research are not initiated prior to IRB approval;
- ensuring prompt reporting to the IRB and FDA of unanticipated adverse events;
- ensuring that investigator noncompliance is addressed;
- suspending or terminating research;
- requiring that a majority of members are present at convened meetings and that at least one member has non-scientific interests; and
- ensuring that a majority of members approve the research.

Failure to prepare and maintain adequate written procedures for performing expedited review according to 21 CFR 56.110.

The current written procedures for handling expedited reviews are inadequate in that they do not include a list of research that may be approved using this procedure and do not include a procedure for informing the full committee of the research approved by expedited review.

Failure to maintain adequate records as required by 21 CFR 56.115.

- The inspection report shows that minutes of meetings do not indicate the members voting for, against, or abstaining from a proposal as required by 21 CFR 56.115(a)(2).

- The inspection report shows that the IRB has failed to document the information in 21 CFR 56.115(a)(5) for each of the IRB members. The list of IRB members maintained by the IRB should clearly indicate the employment or other relationship between each member and the institution. The current membership list does not identify any community representative and does not designate the voting and non-voting members. The membership roster should be updated as necessary to remain current in order to assure that the "quorum" requirements of 21 CFR 56.108(c) are met.

- The IRB granted an extension to [redacted] clinical investigator for the [redacted] in July 1998. However, there were no records of meeting minutes to document that the IRB reviewed the study protocol or that [redacted] submitted a Continuing Approval request to the IRB. There was no record that a protocol amendment dated October 1997 for the [redacted] was approved by the IRB.

- For the "[redacted]" initially approved in February 1999, there were no meeting minutes available to confirm that the IRB held a meeting in July 1999 to approve additional investigators for the study. Also, there was no documentation to show that a protocol change was approved by the IRB in a January 1999 meeting prior to final approval. An annual report for the study was due in February 2000; however, there was no documentation available that the IRB received or requested an annual report for the study.

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. Failure to respond could result in further regulatory actions. 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 action 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 Dallas District Office, 3310 Live Oak, Dallas, Texas 75204. 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,

Charmaine Connor, RPh

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

Enclosure

cc:

Michael Carome, M.D.
Compliance Oversight Branch, MSC 7507
Office for Protection from Research Risks
National Institutes of Health
6100 Executive Boulevard, Suite 3B01
Rockville, Maryland 29892-7507