Inspections, Compliance, Enforcement, and Criminal Investigations

Genetics & IVF Institute IRB 12/23/09

Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, Maryland 20993

WARNING LETTER

VIA FEDERAL EXPRESS

DEC 23 2009

David Wise
Chief Executive Officer
Genetics & IVF Institute
3015 Williams Drive. Suite 101
Fairfax. VA 22031

Dear Mr. Wise:

This Warning Letter is to inform you of the objectionable conditions observed during the Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB) from September 24 to October 1, 2009, by an investigator from the FDA Baltimore District Office (BLT-DO). The purpose of this inspection was to determine whether your IRB is in compliance with applicable federal regulations. IRBs that review investigations of devices must comply with applicable provisions of 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. This letter also requests prompt corrective action to address the violations cited.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions (510(k)) 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.

Our review of the inspection report prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 56 - Institutional Review Boards. At the close of the inspection, the FDA investigator presented an inspectional observations form FDA 483 for your review and discussed the observations listed on the form with you, Dr. Wayne S. Stanley, Genetics and IVF Institute IRB Chair, Miss Mary Sands, the IRB Coordinator and Mr. Daniel Molina, Consultant, Technical Resources Institute (TRI). The deviations noted on the FDA 483 and our subsequent review of the inspection report are discussed below:

1. Failure to conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. [21 CFR 56.109(f) and 56.115(a)(3)]

IRBs shall conduct continuing review of research at intervals appropriate to the degree of risk, but not less than once per year. In addition, the IRB is required to maintain adequate documentation of IRB activities, including records of continuing review activities. Examples of your failure to meet this requirement include, but are not limited to, the following:

• There is no documentation to demonstrate that the IRB conducted continuing review from October 2002 to February 2005 although the **(b)(4)** study was on-going and under the oversight of the IRB during that time.

2. Failure to prepare and maintain minutes of IRB meetings in sufficient detail. [21 CFR 56.115(a)(2)]

The IRB shall 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, and the votes of these actions including the number of members voting for,
against, or abstaining. Listed below are several examples of how you have failed to meet this requirement:

• The available meeting minutes from May 2000 through July 2009 do not consistently list the members in attendance nor do they include, for particular items being reviewed, the number of members voting for, against or abstaining.

• The IRB sent a letter **(b)(4)**, dated June 18, 2009, which stated that various protocols were previously approved on specific dates. However, the approval dates listed in the letter do not correspond with the dates of past IRB meetings. For example, the June letter stated the following:

i) Protocol Number: 0001, Version Number 2, was approved on November 15, 2002, however, according to the roster of IRB meeting dates, the IRB met on September 26, 2002.
ii) Protocol Number: 0001, Version Number 3, was approved on February 4, 2004, however, according to the roster of IRB meeting dates, the IRB did not meet at all in 2004.
iii) Protocol Number: 0001, Version Number 4, was approved on April 5, 2007, however, according to the roster of IRB meeting dates, the IRB met on July 16, 2007.

• The **(b)(4)** program was due for review and approval in March 2006; however, it did not occur until June 2006, three months later. A letter dated June 26, 2006, to **(b)(4)**, Primary Scientific Investigator, states that the IRB reviewed and approved this study at its last IRB meeting. According to the IRB meeting. According to the IRB's documented roster of meeting dates, "the last" IRB meeting would have been March 30, 2005.

3. Failure to adopt a method for keeping all members advised of research proposals which have been approved under an expedited review procedure. [21 CFR 56.110(c)]

Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure. You have failed to meet this requirement in the following way:

• Expedited review and approval of status reports for the **(b)(4)** took place on the following dates: June 4, 2002; July 9, 2003; and June 30, 2004. However, there is no documentation to demonstrate that the IRB members were notified of these approvals.

4. Failure to ensure that no IRB member participates in the initial or continuing review of any projects in which the member has a conflict of interest. [21 CFR 56.107(e)]

No IRB may have a member participate in the IRB's initial or continuing review of any project, in which the member has a conflicting interest, except to provide information requested by the IRB. You failed to adhere to the above stated regulation. Examples of this failure include, but are not limited to, the following:

• At the May 17, 2001 and September 26, 2002 IRB meetings, **(b)(4)**, a principal investigator and then Chairman of the IRB, was present during the review of three studies in which he had a conflicting interest. There is no documentation in the minutes that Dr. Opsahl refrained from voting on the approval of these three studies.

5. Failure to prepare and maintain adequate documentation of IRB activities, including a list of IRB members identified by name; earned degrees; representative capacity; indications of experience; and any employment or other relationship between each member and the institution. [21 CFR 56.115(a)(5)]

An IRB shall prepare and maintain adequate documentation of IRB activities, including a list of IRB members identified by name; earned degrees; representative capacity; indications of experience, and any employment or other relationship between each member and the institution. You failed to adhere to the above stated regulation from 2000 to 2009. Examples of your failure include, but are not limited to, the following:

• There were only three rosters available for review during the inspection. One was undated, one was dated January 13, 1999, and another was dated July 3, 2009. The undated and January 1999 rosters do not identify members' representative capacity and employment or other relationship between members and the institution.

• Two new IRB members, **(b)(4)** and **(b)(4)** were introduced at the July 16, 2007 IRB meeting and both were recorded as present in the July 29, 2007 meeting minutes. Additionally, the July 16, 2007 meeting

minutes record **(b)(4)** as an IRB member as well. However, these members do not appear on a roster until July 3, 2009.

As a result of your IRB's non-compliance with FDA regulations, as described above, FDA hereby directs that no new subjects be enrolled into ongoing studies subject to 21 CFR Part 56 that are reviewed by your IRB, as provided by 21 CFR 56.120(b)(2). This restriction will remain in effect until FDA has evidence of adequate corrective actions and notifies you in writing that the IRB's corrective actions are satisfactory. In addition, FDA may withhold approval of new studies subject to 21 CFR Part 56 that are reviewed by your IRB, as provided by 21 CFR 56.120(b)(1).

The violations described above are not intended to be an all inclusive list of problems that may exist at the IRB. The IRB is responsible for ensuring compliance with the Act and applicable regulations.

Within **fifteen (15) working days** of receiving this letter, please provide **written documentation** of the actions you have taken or will take to correct these violations and prevent the recurrence of similar violations. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to the IRB. Please send your response to: Attention: Linda Godfrey, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 10903 New Hampshire Avenue, Building 66 Room 3462, Silver Spring, MD 20993.

A copy of this letter has been sent to Baltimore District Office, 6000 Metro Drive, Suite 101, Baltimore, Maryland 21215. Please send a copy of your response to that office.

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. The Division of Bioresearch Monitoring has developed introductory training modules in FDA regulated device clinical research practices, which are available on the FDA website.

The modules are for persons involved in FDA regulated device clinical research activities. These modules are located at the following website address:http://www.fda.gov/Training/CDRHLeam/ucm1620l5.htm

If you have any questions, please contact Ms Linda Godfrey, by telephone at (301) 796-5490 or by email at Linda.Godfrey@fda.hhs.gov.

Sincerely,

/s/

Timonthy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

cc:

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