Inspections, Compliance, Enforcement, and Criminal Investigations

Staten Island University Hospital IRB

Department of Health and Human Services

Public Health Service
Food and Drug
Administration
Center for Devices and
Radiological Health
9200 Corporate Blvd
Rockville, MD 20850

WARNING LETTER

JUN 29 2009

Brahim Ardolic, M.D.
Chairperson
Staten Island University Hospital
Institutional Review Board
500 Seaview Avenue
Staten Island, New York 10305-2200

Dear Dr. Ardolic:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection of your Institutional Review Board (IRB) from March 16, 2009, through April 3, 2009, by an investigator from the FDA New York District Office. 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 C.F.R.) Part 56-Institutional Review Boards, Part 50-Protection of Human Subjects, and Part 812-Investigational Device Exemptions. This letter also requests prompt corrective action to address the violations cited. This letter also acknowledges your response dated May 18,2009,

and 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 21 C.F.R. Part 50 -- Protection of Human Subjects, and 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. The deviations noted on the FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

Failure to require that information given to subjects as part of informed consent is in accordance with 21 CFR 50.25 [21 CFR 50.25(a) and 21 CFR 56.109(b)].

An IRB shall require that information given to subjects as part of informed consent is in accordance with 21 CFR 50.25. The IRB failed to ensure that informed consent documents contain all the information required by 21 CFR 50.25. You failed to adhere to the above stated regulations. Examples of your failure include, but are not limited to, the following:

The previous versions as well as the most recent informed consent forms (ICF) dated "Approved 10/8/08 to 10/7/09" applicable to **(b)(4)** did not contain the following elements:

- statements notifying subjects of the purposes of the research and the expected duration of the subject's participation;
- a description of the procedures to be followed;
- a description of any benefits to the subjects or to others which may reasonably be expected from the research; and
- an explanation as to whether any compensation and any medical treatment are available if injury occurs, and if so, what they consist of, or where further information may be obtained.

In your response, you acknowledge that the consent form approved for **(b)(4)** was lacking elements of informed consent. You noted that the IRB accepted a consent form developed by the sponsor in 1997 and that this is an isolated incident as the deficiencies were not found in other consent forms reviewed. Your response is inadequate in that although you have amended the informed consent to include the missing elements, there is no evidence that subjects were re-consented with the amended informed consent form.

Please note that, in addition to not adhering to the requirements for informed consent in 21 CFR 50.25(a), the informed consent for this study did not adhere to your **(b)(4)** in which you describe what elements are needed in the informed consent documents given to subjects.

Failure to follow written procedures for conducting initial and continuing review of research. [21 CFR 56.108(a)]

An IRB shall follow its written procedures for conducting its initial and continuing review of research. You failed to adhere to the above stated regulation. Examples of your failure include, but are not limited to, the following:

The **(b)(4)** subsection entitled, **(b)(4)** states that "a project may be reviewed annually for up to five years following initial approval. After that time, the protocol must be submitted to the IRC for review as a new protocol."

(b)(4) entitled, **(b)(4)** was initially approved on **(b)(4)** and six years later on **(b)(4)** was approved via continuing review. The 2003 approval via continuing review does not conform to the IRB's written procedure, which requires that studies lasting more than five years be reviewed as new studies.

In your response, you indicated that "the requirement for treating a protocol as a new study after 5 years was modeled on a policy at our parent institution, the North Shore-LIJ Health System, but was never fully implemented as it is not a federal requirement." You noted that the IRB policies and procedures are presently being revised and the policy regarding a study being treated as a new study after five years will be removed. Your response is inadequate, in that you did not provide evidence of the corrective and preventative measures that you have taken to prevent the above deviations from recurring in future FDA-regulated studies. Please provide us with documentation of a corrective

action plan for ensuring compliance with your standard operating procedures (SOPs) and applicable federal regulations such as; written verification of training received by you and your study staff applicable newly implemented review procedures as well as copies of the written SOPs.

Failure to ensure that the IRB reviews proposed research at convened meetings at which a majority of the members are present, including at least one member whose primary concerns are in nonscientific areas [21 CFR 56.108(c)].

A majority of members, including at least one member whose primary concerns are in nonscientific areas, is needed to review proposed research at convened meetings. You failed to adhere to the above stated regulation. An example of your failure includes, but is not limited to, the following:

- The **(b)(4)** minutes revealed that the IRB approved research at a convened meeting without a majority of members present. Please note that members with a conflicting interest do not count towards the majority. 21 CFR 56.107(e). The minutes for this meeting indicated that 13 of 25 total voting members listed on the September 26, 2006 IRB member roster were present. There were seven studies under review for which an IRB member had a conflicting interest (i.e. served as a principal investigator), and so did not participate in the review; the IRB nonetheless reviewed and approved these studies, despite the absence of a majority.

In your response, you indicated that the meeting of **(b)(4)** had 24 voting members on the roster. Thirteen voting members were present with two members whose primary concerns are nonscientific, and as a result you believe a quorum was maintained at this meeting for the review of new studies, continuing reviews and full board amendments. Your response is inadequate in that a quorum was not met because 2 of the 13 voting members served as principal investigators for studies that were being reviewed, hence, do not count toward the quorum. Please provide us with documentation of a corrective action plan to address this violation. Please provide in your response, written verification of training received by you and your study staff applicable newly implemented study procedures and copies of written SOPs.

Failure to prepare and maintain accurate and complete documentation of IRB activities. [21 CFR 56.115(a)(4) and (a)(5)].

An IRB shall prepare and maintain adequate documentation of IRB activities, including copies of all correspondence between the IRB and the investigators and 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 regulations. Examples of your failure include, but are not limited to, the following:

- Meeting minutes dated **(b)(4)** lists doctors **(b)(4)** and **(b)(4)** as members who were present at the meeting. However, neither is listed on the **(b)(4)** IRB roster (submission number 13586) as a voting member.

- A research study titled, **(b)(4)** was approved by the IRB on **(b)(4)** pending changes to the informed consent. There is no documentation or other evidence of these changes being submitted to the IRB. The IRB apparently approved this study anew on **(b)(4)** There is no documentation of the correspondence between the IRB and principal investigator regarding the **(b)(4)** approval.

- The membership roster dated **(b)(4)** lists **(b)(4)** as a nonscientific member. **(b)(4)** obtained a Bachelor's Degree in Biology in **(b)(4)** as well as a Masters in Public Health in **(b)(4)** and appears to be involved in scientific areas. She should be listed as a scientific member.

In your response, you also indicated that the letter informing the PI of the return of the protocol in **(b)(4)** is missing from the IRB files due to water damage to the IRB Office in February 2005. Your response is inadequate in that you have not provided documentation of a corrective action plan for ensuring compliance with applicable federal regulations. Please provide documentation (e.g. SOPs) elucidating how study files will be stored and/or protected during similar incidents that may occur in the future.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a clinical investigator to ensure 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 you.

You will find information to assist you in understanding your responsibilities and planning your corrective actions in the FDA Information Sheets Guidance for Institutional Review Boards and Clinical Investigators, which can be found at http://www.fda.gov/oc/ohrt/irbs/. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Send your response to: Attention: Mr. G. Levering Keely, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-31O, Rockville, Maryland 20850
A copy of this letter has been sent to Joy P. Matthias, New York District Office, 158-15 Liberty Avenue, Jamaica, New York 11433. Please send a copy of your response to that office.

If you have any questions, please contact Levering, Keely, BSN, MPA, at 301-796-5663 or via e-mail at Levering.Keely@fda.hhs.gov.

Sincerely yours,

/S/
Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

Cc:
Anthony Ferri, President, Chief executive Officer
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Kristina C. Borror, Ph.D.
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