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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
9200 Corporate Boulevard
Rockville, Maryland 20850

WARNING LETTER

VIA FEDERAL EXPRESS

John S. Bowling
CEO
Hamilton Medical Center
1200 Memorial Drive
Dalton, Georgia 30720

SEP 2 2008

Dear Mr. Bowling:

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 May 20 to May 28, 2008 by an investigator from the FDA's Atlanta 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 acknowledges receipt of Mrs. Beverly Joy, RN, IRB Facilitator's June 3, 2008 response to the form FDA 483 "Inspectional Observations," discusses the written response to the noted violations, 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 Title 21, Code of Federal Regulations (21 C.F.R.) Part 56-Institutional Review Boards. At the close of the inspection, the FDA investigator presented an inspectional observations form FDA 483 to Dr. Carlton Lancaster, IRB Chairman and Mrs. Joy, for review and discussed the observations listed on the form. The deviations noted on the FDA 483, your written response and our subsequent review of the inspection report are discussed below:

Failure to have adequate written procedures governing the functions and operations of the IRB [21 CFR 56.108 (a) and (b)].

An IRB must prepare, maintain and follow written procedures that describe the IRB's functions and operations, including: conducting continuing review of research; determining which projects require review more often than annually, and which projects need verification from sources other than the investigator that no material changes have occurred since

previous IRB review; ensuring that changes to approved research may not be initiated without IRB review and approval, except where necessary to eliminate apparent immediate hazards to the human subjects; and ensuring prompt reporting to the IRB, appropriate institutional officials, and the FDA of unanticipated problems involving risks to human subjects. The "Hamilton Medical Staff Policy," dated October 2005, lacked procedures for the following requirements:

- Continuing review of research and for reporting its findings and actions to the institution and the investigator;

- Determining which projects require review more often than annually and for projects that need verification from sources other than the investigator that no material changes have occurred since previous IRB review; and

- Ensuring prompt reporting to the IRB of changes in research activities; and for ensuring prompt reporting to the IRB, institutional officials, and the FDA of unanticipated problems involving risks to human subjects, of instances of noncompliance with regulations, and of suspension or termination of IRB approval.

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

Pursuant to 21 CFR 56.108(c), a majority of members, including at least one member whose primary concerns are in the nonscientific area 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 IRB membership list for 2003 consists of [redacted] members. During the meeting that occurred on March 18, 2003, the IRB reviewed and approved the "[redacted]" study; however, the minutes of the meeting document that only 7 of the [redacted] IRB members were present.

Failure to conduct continuing review of research at least annually [21 CFR 56.109(f)].

Pursuant to 21 CFR 56.109(f), an IRB shall conduct continuing review of FDA regulated research at intervals appropriate to the degree of risk, but not less than once per year. Examples of your failure include, but are not limited to, the following:

- The "[redacted]" study received initial approval on March 18, 2003; however, continuing review was not performed until June 1, 2004. In addition, there was no documentation that continuing review for 2006 was performed, and there is no documentation that the study was suspended during that time.

Failure to prepare and maintain adequate documentation of IRB activities, including copies of all meeting minutes and lists of IRB members in sufficient detail [21 CFR 56.115(a)(2) and 56.115(a)(5)].

Pursuant to 21 CFR 56.115(a)(2), minutes of IRB meetings shall be maintained in sufficient detail to show attendance at the meeting and actions taken by the IRB to include the number of members voting for, against, or abstaining. In addition, pursuant to 21 CFR 56.115(a)(5), an IRB shall prepare and maintain a list of IRB members identified by name, earned degrees, representative capacity, and the 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:

- The meeting minutes dated March 18, 2003, [redacted], and [redacted] do not show the number of members who voted for, against or abstained. The minutes do not include details related to the presence or absence of members with a conflict of interest and whether these members participated in the review and voted.

- The [redacted] minutes do not show who attended the meeting.

- There were no meeting minutes available for [redacted], and [redacted] And

- The membership rosters for 2003, 2004, 2006, 2007, and April 2008 do not identify the earned degree, representative capacity, and relationship between each member and the institution.

Mrs. Beverly Joy's response states that the following new processes are already in place:

- Hamilton Medical Center recently appointed new IRB members as well as a new chairman;

- The IRB registered with the Office for Human Research Protections (OHRP);

- The hospital administration appointed a RN facilitator to record minutes during the IRB meeting; and

- The IRB will meet in July to review the IRB organizational policy and develop new policies and procedures to meet the standards brought to their attention during the FDA inspection.

Your response is inadequate in that it does not include documentation of the following: new or revised policies and procedures related to continuing review, reporting findings and actions, frequency of review, and how the IRB handles changes in research activities, prompt reporting of unanticipated problems, non-compliances, and suspension or termination of studies; documented dates of training for staff and list of staff trained; and timelines for

implementation of the corrective actions suggested. In addition, include with your response to this letter a description of any new or revised processes and procedures implemented to ensure a majority of members are present when conducting initial and continuing review, ensuring continuing review conducted at intervals appropriate to the degree of risk, and ensuring preparation and maintenance of detailed minutes and a list of IRB members.

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 you. Send your response to: Attention: Ms. Linda Godfrey, Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 9200 Corporate Boulevard, HFZ-310, Rockville, Maryland 20850.

A copy of this letter has been sent to Atlanta District Office, 60 Eighth Street, NE, Atlanta, Georgia 30309. Please send a copy of your response to that office.

If you have any questions, please contact Ms. Linda Godfrey at (240) 276-0125 or via email at Linda.Godfrey@fda.hhs.gov.

Sincerely yours,

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