

# **Inspections, Compliance, Enforcement, and Criminal Investigations**

## **McLaren Regional Medical Center Institutional Review Board 1/14/2008**



Department of Health and Human Services

Public Health Service  
Food and Drug  
Administration  
9200 Corporate Boulevard  
Rockville, Maryland 20850

**JAN 14, 2008**

### **WARNING LETTER**

VIA FEDERAL EXPRESS

Donald Kooy  
Corporate Executive Officer  
McLaren Regional Medical Center  
Institutional Review Board  
401 South Ballenger Highway  
Flint, Michigan 48532-3638

Dear Mr. Kooy:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your Institutional Review Board (IRB) from August 8, 2007 through August 30, 2007 by an investigator from the FDA Detroit 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 and discusses your written response dated September 18, 2007 to the noted violations.

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 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 assure that documentation of and information given to the subjects as part of the informed consent include all required information or elements in accordance with 21 CFR Part 50.25 (21 C.F.R. 56.109(b)).**

In accordance with 21 CFR Parts 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. In seeking informed consent, the following information shall be provided to each subject: a statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the FDA may inspect the records as per 21 CFR 50.25(a)(5).

The informed consents did not contain statements notifying subjects of the possibility that the FDA might inspect their records for the following studies: **(b)(4)** dated April 15, 2005; and the **(b)(4)** dated November 18, 2005.

Your response states that the IRB will revise the informed consent checklist to prevent this violation from recurring. Please provide a copy of the revised informed consent checklist you have implemented as well as a timeline for implementation of the checklist.

**Failure to follow required written procedures in accordance with 21 CFR Part 56.108(a) and failure to ensure adequate continuing review and conduct continuing review of research in accordance with 21 CFR Part 56.109(e) and (f).**

Pursuant to FDA regulations 21 CFR Parts 56.108(a) and 56.109, IRBs shall follow

written procedures for conducting initial and continuing review of research, review and in (to secure approval), or disapprove all research activities covered by these regulations. IRBs shall notify investigators and the institution in writing of its decision to approve or disapprove research activity, and conduct continuing review of research covered by these regulations at intervals appropriate to the degree of risk, but no less than once per year. The McLaren Regional Medical Center IRB **(b)(4)** on August 28 2002, states that **(b)(4)**. Examples of the IRB's failure to adhere to the above stated regulations as well as follow its procedures include but are not limited to the following:

The informed consent document (ICD) for **(b)(4)** entitled, **(b)(4)** was initially approved on December 21, 2001 pending inclusion of a statement that explains to the subject that significant findings related to the subject's treatment will be discussed with the subject, as well as the inclusion of the correct listing of all contact numbers. However, there is no documentation indicating that the clinical investigator had completed the modifications, and that the IRB reviewed and approved the modified ICD. Additionally, documentation reflects that continuing review for study **(b)(4)** had lapsed for over **(b)(4)** and **(b)(4)**, from **(b)(4)**.

For study **(b)(4)**, the continuing review application approved by the IRB on September 15, 2006, documents that subject experienced a serious adverse event, femoral nerve palsy, on March 13, 2006, during the time of surgery. The investigator stated that the femoral nerve palsy was not related to the device; however, the IRB did not acknowledge this as a serious adverse event (SAE), did not perform any independent investigation as to whether the SAE was unrelated to the device, and did not inquire about why the SAE was not reported to the IRB within the 30 day timeframe requirement for reporting SAEs that are study unrelated as reflected in McLaren Regional Medical Center IRB **(b)(4)**.

Your response indicates that you will enforce existing continuing review policy and implement renewal notice process with new software to proactively identify studies prior to the renewal expiration. You also stated that non-compliance with your policy by Principal Investigators (PIs) will result in immediate closure of their studies and that there will be a notice to the PI by registered mail. Your response is inadequate in that it does not reflect evidence of any training provided to the IRB members regarding enforcement of the IRB's policy.

### **Failure to adhere to IRB membership requirements 21 CFR Part 56.107(f).**

In accordance with 21 CFR 56.107 (f), an IRB may, at its discretion, invite individuals with competence in special areas to assist in the review of complex

issues which require expertise beyond or in addition to that available on the IRB. But these individuals may not vote with the IRB. There were several instances which the IRB invited individuals with competence in a special area to assist in the review of complex issues, and allowed those individuals to vote. Examples of your failure to adhere to the above stated regulation include but are not limited to the following:

The May 19,2006, meeting minutes documented that **(b)(6)** substituted as a voting member for **(b)(6)**. However, **(b)(6)** is not listed as an IRB member on any of McLaren Regional Medical Center IRB rosters. Similarly, the July 20,2007 meeting minutes reflects that **(b)(6)** substituted as a voting member for **(b)(6)**, and substituted as a voting member for **(b)(6)**; however, neither **(b)(6)** nor is listed on the main roster or alternate list as members of the IRB.

Meeting minutes dated May 20,2005, listed **(b)(6)**, as a voting member of the IRB; however, the IRB rosters do not reflect that **(b)(6)** is a member of the IRB.

Your response indicated that the designated alternate list will be reviewed and revised as needed to include all identified alternates, and that the IRB will review and approve them as members. You also indicate that you will educate all IRB members regarding the requirements for voting eligibility. Please provide documentation of the revised alternate list and the training provided to the IRB members on the voting requirements.

#### **Failure to prepare and maintain adequate documentation of IRB activities 121 CFR Part 56.115].**

In accordance with 21 CFR 56.115(a)(1) and 56.115(a)(3) an IRB shall prepare and maintain adequate documentation of IRB activities. including copies of all research proposals reviewed; progress reports submitted by the investigators; the basis for requiring changes in or disapproving research; minutes of IRB meetings which shall be in sufficient detail to show attendance at all meetings, actions taken by the IRB, the vote on these actions, and a list of members. Examples of your failure to adhere to the above stated regulation include but are not limited to the following

The **(b)(4)** was missing its initial IRB application, as well as continuing review documents from **(b)(4)**. Similarly, records of continuing review activities were missing for study file **(b)(4)**.

The IRB file for **(b)(4)** was missing several documents including the original IRB review letters, the IRB's letter of study suspension, a revised version of the informed consent, and the protocol.

The IRB file for **(b)(4)** was missing the study's initial approval application as well as the protocol.

Your response indicates that you will begin to implement ongoing, semi-annual, random file audits to ensure file organization is maintained. Also, your response states that during the progress of studies, letters will be corrected and resent to investigators to ensure that study files are accurate and complete. Your response is inadequate in that you did not provide evidence of training provided to IRB members/study coordinator regarding file maintenance and/or evidence of the letters sent to the investigators to correct file inaccuracies.

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.

Please note that your roster lists alternate members, as non-scientific members; however, review of curriculum vitae reflects that these members hold scientific degrees. We recommend that you revise your roster to reflect appropriate designations. Please refer to the website at, <http://www.fda.aov/oc/ohrt/irbs/default.htm>. Appendix H entitled, "A Self-evaluation Checklist for IRBs" for guidance on ensuring sufficient written procedures for conducting IRB review of FDA-regulated research.

Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional 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-312, Rockville, Maryland 20850.

Your failure to adequately respond to this letter may result in further administrative actions against your IRB, as authorized by 21 CFR 56.120 and 56.121. These actions include FDA withholding approval of new studies reviewed by your IRB that are subject to Parts 50 and 56 of the FDA regulations, prohibiting the admission of new subjects to ongoing studies that are subject to 21 CFR Parts 50 and 56, terminating all ongoing studies approved by your IRB, and initiating regulatory proceedings for disqualification of your IRB.

A copy of this letter has been sent to New England District Office, One Montvale Avenue, 4th floor, Stoneham, Massachusetts 02180. Please send a copy of your response to that office.

If you have any questions, please contact Linda Godfrey, at 240-276-0125 or via

e-mail at [Linda.Godfrey@fda.hhs.gov](mailto:Linda.Godfrey@fda.hhs.gov).

Sincerely yours,

Timothy A. Ulatowski  
Center for Devices and  
Radiological Health