



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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Food and Drug Administration
Center for Biologics Evaluation and Research
1401 Rockville Pike
Rockville MD 20852-1448

By Certified Mail – Return Receipt Requested
And by Facsimile Transmission

CBER – 06 – 005

Warning Letter

James Nesselroad, M.D., IRB Chairperson
Galesburg Institutional Review Board
3333 N. Seminary Street
Galesburg, Illinois 61401

Dear Dr. Nesselroad:

This letter describes the results of a Food and Drug Administration (FDA) inspection that was conducted from February 13 through 21, 2006. FDA investigator Susan D. Yuscious conducted an inspection of Galesburg Institutional Review Board (IRB) to determine if the IRB's procedures for the protection of human subjects comply with FDA regulations published in Title 21, Code of Federal Regulations (CFR), Parts 50 and 56. FDA conducted this inspection under the agency's Bioresearch Monitoring Program, which includes inspections designed to review IRB operations for clinical studies using investigational products, and for the protection of human subjects.

At the end of the inspection, a Form FDA 483, Inspectional Observations, was issued and discussed with you and other staff members of St. Mary Medical Center and Galesburg Cottage Hospital.

We received the letter dated February 24, 2006, from [REDACTED]
[REDACTED] Galesburg Cottage Hospital, and [REDACTED]
[REDACTED] St. Mary Medical Center in response to the Form
FDA-483. The letter includes revised IRB standard operating procedures dated
02/10/06. Our comments on that response to the Form FDA-483 are included below.

We have determined that the IRB significantly violated regulations governing the operation and responsibilities of IRBs as published under 21 CFR 50 and 56 (available at <http://www.gpoaccess.gov/cfr/index.html>). The applicable provisions of the CFR are cited for each violation. We acknowledge that you were not elected IRB Chairperson until February 3, 2006, and therefore you were not personally responsible for the IRB's failure to comply with regulatory requirements before then. We are addressing this letter to you under 21 CFR 56.120(a) as the current IRB Chairperson with responsibility for ensuring that the IRB takes the actions necessary to bring the IRB into full compliance with FDA regulations. Under 21 CFR 56.120(a) we are also sending copies of this letter to the responsible heads of the IRB's two parent institutions, Galesburg

Cottage Hospital and OFS St. Mary Medical Center, because under 21 CFR 56.120(c), parent institutions are presumed to be responsible for an IRB's operations.

1. **The IRB failed to prepare, maintain, and follow adequate written procedures for conducting its initial and continuing review of research. [21 CFR §§ 56.108(a) and (b), and 56.115(a)(6)].**

The IRB's written procedures dated April 1993, which the IRB used for the initial and continuing review of research involving human subjects from April 1993 through February 21, 2006, were not adequate for a number of reasons, including but not limited to the following:

- They did not specify how members were to be selected to ensure the composition of the IRB met all regulatory requirements for IRB membership.
- They included no instructions for conducting continuing review of studies.
- They did not specify how the IRB would determine whether a research study involved a significant risk device.
- They stated that all open studies were to be reviewed [REDACTED]
- They failed to state how the IRB would consider research proposed by IRB members.

The IRB approved revised written procedures on February 10, 2006, just prior to the start of this inspection. The revised procedures are much more detailed, and correct most of the previous deficiencies. They are still inadequate, however, in at least the following ways:

- The revised procedures do not indicate if ad hoc members have voting privileges.
- The revised procedures do not address maintaining a roster of current IRB members as required by 21 CFR 56.115(a)(5).
- The revised procedures do not address how the IRB will determine whether a research study involves a significant risk device. 21 CFR Part 812.66.

We request that, in addition to making those specific corrections, you thoroughly review your revised procedures to ensure that, as implemented, they comply with all FDA requirements.

2. **The IRB failed to review proposed research at convened meetings at which a majority of the members of the IRB were present, including at least one member whose primary concerns are in nonscientific areas. [21 CFR § 56.108(c)].**

- A. The IRB voted on and approved new protocols, reviewed reports of adverse events, and conducted periodic review of studies without the majority of IRB members in attendance. For example:

IRB members listed on roster	Meeting date(s)	Members in attendance	Quorum	Voted on new Protocols
25 members	4/5/02	12 members	NO	YES
	12/6/02	8 members		
20 members	2/7/03	9 members	NO	YES
	2/14/03	8 members		
11 members	10/1/04	5 members	NO	YES
	11/5/04	4 members		
10 members	3/2/05	4 members	NO	YES
	4/1/05; 6/3/05; 8/5/05; 11/11/05; 12/2/05	5 members		

- B. The meeting minutes for February 7 and 14, 2003, document that the IRB did not have a nonscientific member present when the IRB approved new research proposals and approved continuation of studies.

In the letter dated February 24, 2006, the IRB states that additional members have been recruited, and that following the revised procedures should prevent similar problems in the future. The corrective action is inadequate as it does not indicate what, if any, action that IRB has taken or plans to take in regard to the studies that were reviewed, voted on, and approved without the benefit of a quorum and a nonscientific member present. In addition to stating what actions the IRB will take on open studies that the IRB approved without the benefit of a quorum and nonscientific member present, we request that you also review closed studies of FDA-regulated products to determine whether any were approved without the benefit of a quorum and nonscientific member present. We request that you notify FDA of the outcome of your review, and any actions you take as a result, such as notifying sponsors of any deficiencies you found.

3. **The IRB failed to conduct continuing review of research at intervals appropriate to the degree of risk. [21 CFR § 56.109(f)].**

During a meeting held on 2/6/04, the IRB approved the study titled [REDACTED]. Subsequent to the initial approval, there have been significant revisions to both the protocol and the informed consent document. This study has not been subject to continuing review since the initial approval of 2/6/04.

As stated in the IRB's letter dated February 24, 2006, the proposed corrective action is to conduct an immediate review of the study. In your response to this

letter, please provide information as to your findings, and what specific actions the IRB took regarding this study.

4. **The IRB failed to determine that approved studies are consistent with sound research design, and do not unnecessarily expose subjects to risks. [21 CFR § 56.111(a)(1)].**

As part of its normal operations, the IRB approved studies without receiving or reviewing the full study protocol, investigator's brochure, or informed consent documents. The IRB's approval of proposed research and the associated informed consent documents was based solely on information that was provided in a study synopsis, not the full protocol or actual informed consent documents.

In the letter dated February 24, 2006, the IRB promised to conduct a 100% review of all open studies. In your response to this letter, please provide an estimated completion date of the 100% review of all open studies subject to Parts 50 and 56 of the FDA regulations. If the review has already been completed, please provide documentation of the review, including a summary discussion of any controverted issues and their resolution; all actions taken by the IRB, and the vote on those actions, including the number voting for, against, and abstaining.

5. **The IRB failed to prepare and maintain adequate documentation of IRB activities. [21 CFR §§ 56.115(a)(2) and 56.115(a)(5)].**

- A. The IRB's meeting minutes for the period of April 2001 through February 2006 do not always record a summary discussion of controverted issues and their resolution, and are not in sufficient detail to show all actions taken by the IRB, and the vote on those actions, including the number voting for, against, and abstaining.
- B. A letter dated 2/1/02 documents that the IRB approved the continuation of the [REDACTED] study during a meeting of the IRB on 2/1/02. However, there were no meeting minutes to document that the full board met on 2/1/02.
- C. The IRB failed to maintain a roster of all current IRB members to include: name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations, and employment or other relationship between each member and the institution. Although the 2006 membership roster contains more information than the previous versions, it did not contain information sufficient to describe each member's chief or anticipated contributions to IRB deliberations, nor did it contain information on employment or other relationship between each member and the institution.

6. **The IRB failed to require that information given to subjects as part of informed consent is in accordance with the provisions of 21 CFR § 50.25. [21 CFR § 56.109(b)].**

The consent form for the [REDACTED] study lacks the following element required by 21 CFR 50.25: an explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

We recommend that you expand the written procedures to explain how the IRB will determine if an IND or IDE is required. Sections 5.1 and 5.2 in the revised procedures, state that the investigator is responsible for indicating whether an Investigational New Drug application (IND) or Investigational Device Exception (IDE) is required. The IRB may wish to verify that the clinical investigator's conclusion is correct.

This letter is not intended to be an all-inclusive list of deficiencies in the operations of the IRB.

Please notify this office in writing, within fifteen (15) business days of receipt of this letter, of the actions you have taken or plan to take to bring the IRB into compliance with FDA requirements. Please provide the requested information, and include a copy of any revised documents, such as written procedures and a revised roster with your response. Also, for any plans of action, please include the projected completion dates for action to be accomplished.


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 could include FDA prohibiting the approval by your IRB of new studies 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.

Please send your written response to:

Robert L. Wesley
Division of Inspections and Surveillance (HFM-664)
Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research
1401 Rockville Pike, Suite 200N
Rockville, MD 20852-1448
Telephone: (301) 827-6348

We request that you send a copy of your response to the FDA Chicago District office listed below.

Sincerely,


for Mary A. Malarkey, Director

Office of Compliance and Biologics Quality
Center for Biologics Evaluation and Research

Cc:

Scott MacIntire, District Director
Food and Drug Administration
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Kristina Borrer, Ph.D., Chief
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