DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

OCT 12 2001

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Ref: 01-HFD-45-0902

Bruce E. Rampage
Chief Executive Officer
St. Anthony Memorial Health Center
301 West Homer Street
Michigan City, Indiana 46360

Dear Mr. Rampage:

Between January 10 and 19, 2001, Ms. Myra Casey, representing the Food and Drug Administration (FDA), conducted an inspection of the St. Anthony Memorial Health Center Institutional Review Board (IRB). The purpose of this inspection was to determine whether the procedures for the protection of human subjects complied with Title 21 of the Code of Federal Regulations (CFR) Parts 50 and 56 (enclosure #1). These regulations apply to clinical studies of products regulated by FDA.

From our evaluation of the inspection report, the documents submitted with that report, and your written response dated January 26, 2001, we conclude that the IRB failed to adhere to pertinent federal regulations as required by 21 CFR Parts 50 and 56. We note that at the conclusion of the inspection, Ms. Casey presented and discussed with you the items listed on Form FDA 483, Inspectional Observations (enclosure #2). In your letter of January 26, 2001, you failed to adequately address the violations noted on the Form FDA 483. Because your institution plans to proceed with operations, we wish to summarize our findings and emphasize the following:

1. SUMMARY OF VIOLATIONS RELATED TO IRB FUNCTIONS AND OPERATIONS (21 CFR 56.108)

a. The IRB failed to develop, adopt and follow written procedures that specifically describe their function and operation to ensure the following:

- initial and continuing review of research;
- determination of which projects require review more often than annually;
- prompt reporting to the IRB of changes in research activity;

- that changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except where necessary to eliminate apparent immediate hazards to the human subjects;
- prompt reporting to the IRB, appropriate institutional officials, and the FDA of any unanticipated problems involving risks to human subjects or others, any instance of serious or continuing noncompliance with these regulations or the requirements or determinations of the IRB, and any suspension or termination of IRB approval.

b. The IRB failed to review proposed research at convened meetings at which a majority of members are present including one member whose primary concerns are in the non-scientific area. The IRB meeting notice dated 10/24/97 to review the [redacted] Trial documents that the IRB consisted of 6 members, however, in a letter dated 4/20/98, Dr. [redacted] IRB Chairman, notified Duke University that 3 of those 6 members were nonvoting members of the IRB. Therefore, it appears that the [redacted] Trial was approved without the presence of a nonscientific member.

2. SUMMARY OF VIOLATIONS RELATED TO IRB MEMBERSHIP (21 CFR 56.107)

The IRB failed to meet membership requirements in that the IRB did not have at least five members, with varying backgrounds including at least one member whose primary concerns are in nonscientific areas.

3. SUMMARY OF VIOLATIONS RELATED TO IRB RECORDS (21 CFR 56.115)

a. The IRB failed to maintain meeting minutes to document attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. It is noted that the meeting minutes dated 6/18/97 was the only set of minutes provided during the inspection to document that the IRB convened and reviewed research.

b. The IRB failed to maintain documentation of continuing review activities for the following studies: Ribavirin [redacted] Protocol [redacted] The [redacted] Trial [redacted] Protocol [redacted] The [redacted] Trial [redacted] Protocol [redacted] and [redacted] Protocol [redacted]

c. The IRB failed to maintain a list of members identified by name; earned degree; representative capacity; any employment or other relationship between each member and the institution.

Administrative Restrictions

We have no assurance that the IRB activities are adequately protecting the rights and welfare of human subjects of research. For this reason, in accordance with 21 CFR 56.120(b)(1) and (2),

- **no new studies** that are subject to the requirements of this part are to be approved by your IRB, and
- **no new subjects** are to be admitted to ongoing studies that are subject to this part.

These restrictions do not relieve the IRB of its responsibility for receiving and responding to reports of unexpected and serious reactions and routine progress reports from ongoing studies.

Because of the departures from FDA regulations discussed above, please inform this office, in writing, within 15 working days of your receipt of this letter, of the actions you have taken or plan to take to bring the procedures of your IRB into compliance with FDA regulations. Please include a copy of any revised documents, such as written procedures, with your response. Any plans of action must include projected completion dates for each action to be accomplished.

We will review your response and determine whether the actions are adequate to permit the IRB to resume unrestricted activities. 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, but are not limited to, the termination of all ongoing studies approved by your IRB and the initiation of regulatory proceedings for disqualification of your IRB.

Should you have any questions, please contact Dr. Antoine El-Hage, at (301) 594-1032, FAX (301) 827-5290. Your written response and any pertinent documentation should be addressed to:

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Office of Medical Policy
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, Maryland 20855

Sincerely yours,

Joanne L Rhoads MD

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