DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

Warning Letter

OVERNIGHT DELIVERY

Reference #: 98-HFD-340-1101

DEC 3 1997

Richard Hudson, FACHE
President and Chief Executive Officer
St. Francis Hospital, Inc.
2122 Manchester Expressway
Columbus, Georgia 31909

Dear Mr. Hudson:

On August 11, 12 and 18, 1997, Ms. Myla D. Chapman, an investigator with the Atlanta District Office of the Food and Drug Administration (FDA), inspected the St. Francis Hospital, Incorporated - Institutional Review Committee which serves as the institutional review board (IRB). The purpose of this inspection was to determine whether your procedures for the protection of human research subjects complied with Title 21 Code of Federal Regulations (CFR), Parts 50 and 56 (Enclosure #1, Appendices B and C). These regulations apply to clinical studies of products regulated by the FDA.

At the completion of the inspection, Ms. Chapman issued Mr. Michael E. Zielaskiewsicz, Vice President and Chief Nursing Officer, a Form FDA 483, Inspectional Observations (Enclosure #2). Also present during this discussion were Ms. Bonny Yancey, Medical Staff Coordinator; Ms. Francis Reitz, Regulatory Review Officer and Ms. Linda Cormack, Director of Medical Staff Service. Based on our review of the Form FDA 483, Ms. Chapman's written report and the documents collected by her during the inspection, we conclude that the IRB for St. Francis Hospital, Incorporated is in serious violation of the FDA requirements for the protection of human subjects of research. The most serious violations are summarized below.

Failure to have adequate written procedures for IRB functions and operations [21 CFR 56.108]: The Medical Staff Bylaws of St. Francis Hospital, Incorporated, approved by the Board of Trustees, effective March 26, 1996 (Enclosure #3), are completely inadequate as written procedures to describe the functions and operations of an IRB as required by 21 CFR 56.108(a)(1-5) and 56.108(b)(1) and (2) [Form FDA 483, item #1]. Your IRB's written procedures inadequately address the following specific areas:

- conducting initial and continuing review of research and for reporting findings and actions to investigators and your institution, as required by 21 CFR 56.108(a)(1);

- for determining which research 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, as required by 21 CFR 56.108(a)(2);

- for ensuring prompt reporting to the IRB of changes in research activity, as required by 21 CFR 56.108(a)(3); and

- for ensuring 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 human subjects, as required by 21 CFR 56.108(a)(4).

Although your IRB's written procedures are deficient in other areas, we believe the above items represent the most significant violations of 21 CFR Part 56.

Failure to Maintain Adequate IRB Records [21CFR 56.115(a)(2)]:
Your IRB minutes fail to adequately document actions taken and discussed during meetings. The minutes do not identify the results of voting by a numerical tabulation of the votes for both the original and continuing review of studies that are subject to parts 50 and 56 of the regulations, as required by 21 CFR 56.115(a)(2). This violation is listed in part on the FDA 483 in items 2 and 6.

Additionally because of the failure to maintain adequate records as described below we cannot be assured that the following review requirements for initial and continuing review have been performed at your IRB:

IRB's Initial Review [21 CFR 56.109(e)]:
Your IRB failed to maintain documentation of written notification to the clinical investigator and the institution of its decisions to approve or disapprove proposed research activities. The IRB must provide clinical investigators with written descriptions of any modifications which may be required in order to obtain IRB approval to initiate or to continue such research. Your IRB also failed to maintain a copy of the material that had been reviewed (i.e., protocols, informed consent etc.) in making the decision to approve or disapprove the study.

IRB's Continuing Review [21 CFR 56.109(f)]:
The IRB has failed to conduct continuing review at intervals appropriate to the degree of risk, but not less than once a per year. There is no documentation of continuing review of studies at convened meetings in the minutes of the meetings or elsewhere in the IRB's files.

The above observations should not be interpreted as all inclusive. You are responsible for assuring that all FDA regulations are adequately and consistently implemented. A self evaluation of your written procedures can be done by using appendix H in the Information Sheets for Institutional Review Boards and Clinical Investigators (Enclosure 1).

ADMINISTRATIVE RESTRICTIONS: We have no assurance that your institution's practices and procedures 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):

1 no new studies that are subject to Parts 50 and 56 of the FDA regulations are to be approved by your IRB; and

2. no new subjects should be admitted to ongoing studies that are subject to Parts 50 and 56, until this office has assurance that adequate corrections have been made.

These restrictions do not apply to the emergency use of an investigational material when the conditions described in 21 CFR 56.102(d) exist and the procedures followed by your institution fully meet the requirements described in 21 CFR 56.104(c). Neither does this restriction relieve the IRB from receiving and reacting to proposed amendments, reports of unexpected and serious reactions and routine progress reports from ongoing studies.

Please inform this office, in writing, within fifteen (15) working days from the date of receipt of this letter, of the actions you have taken or plan to take to bring the procedures of your institutional review board into compliance with FDA requirements. Plans of action should include projected completion dates for each action to be accomplished. Your failure to adequately respond to this letter, may result in further administrative sanctions being invoked against your IRB, as authorized by 21 CFR 56.120 and 56.121. These sanction may include, but are not limited to, the termination of all previous studies approved by your IRB and the initiation of regulatory proceeding for disqualification of your IRB.

If you have any questions please contact Commander Robert K. Leedham, Jr., USPHS, at telephone number 301-594-1026. Your response should be addressed to:

Anthony E. Rodgers, Acting Team Leader
Human Subject Protection Team HFD-343
Division of Scientific Investigations
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, Maryland 20855

Sincerely yours,

David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
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