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Food and Drug Administration
Rockville MD 20857**WARNING LETTER****OCT - 5 1998****CERTIFIED MAIL**

Ref. No. : 99-HFD-340-0101

Return Receipt Requested

Albert Dicker
CEO
Franklin Hospital Medical Center
900 Franklin Avenue
Valley Stream, New York 11580

Dear Mr. Dicker:

On August 3-12, 1998, Thomas P. Hansen, an investigator with the New York District Office of the Food and Drug Administration (FDA), conducted an inspection of the Franklin Hospital Medical Center (FHMC) Investigational Drug Committee, which serves as the Institutional Review Board (IRB) for your institution. The purpose of this inspection was to determine whether your procedures for the protection of human subjects complied with Title 21, Code of Federal Regulations (CFR), Parts 50 and 56. These regulations apply to clinical studies of products regulated by FDA.

At the conclusion of the inspection, Mr. Hansen issued a Form FDA 483 [enclosed] to Edward S. Orzac, M.D., Medical Director, FHMC, which described the deviations from requirements specified under 21 CFR Parts 50 and 56 that he identified during the inspection. Mr. Hansen also discussed these observed deficiencies with Dorothy Levin, Vice President, FHMC, Peter Giacobelli, R.Ph., Director of Pharmacy, FHMC, and Susan Sayer, R.Ph, Assistant Director of Pharmacy, FHMC.

The Agency has reviewed the documents and records relating to the IRB's responsibilities for the protection of research subjects of research contained in Mr. Hansen's inspection report and the objectionable conditions and practices listed in the current Form FDA 483. The record shows that the IRB has failed to adhere to pertinent federal regulations as contained in 21 CFR Parts 50 and 56. The Agency's findings represent significant violations of the Federal Food, Drug, and Cosmetic Act.

Summary of IRB Functions and Operations Violations [21 CFR 56.108(a)(1)(2)(3)(4), (b)(1)(2)(3) and (c)]:

1. The IRB has failed to develop written procedures for conducting initial and continuing review of ongoing research and for determining which projects require continuing review more often than once a year. [Form FDA 483-item #1]

2. The IRB has failed to assure that clinical investigators are made aware of their reporting responsibilities. There are no written procedures for assuring that investigators promptly report any changes in research to the IRB; for insuring 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 when necessary to eliminate apparent immediate hazards to the subjects; and for insuring that investigators promptly report to the IRB unanticipated problems involving risks to subjects. [Form FDA 483-item #1]

3. The IRB has failed to develop written procedures for insuring 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 FDA regulations or the requirements or determinations of the IRB; and any suspensions or terminations of IRB approval. [Form FDA 483-item #1]

4. The IRB has failed to review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. [Form FDA 483-item #9]

Summary of IRB Records/Membership Violations [21 CFR 56.107(d)(e) and 56.115(a)(1)(2) and (5)]

5. The IRB has failed to include at least one member who is not otherwise affiliated with the institution. [Form FDA 483-item #6]

6. The record of the April 13, 1997 IRB meeting minutes shows that an IRB member, Scott J. Ratner, M.D., who was identified as the principal investigator of a research study submitted for IRB review and approval, failed to abstain from participating in the review and approval of the research study. [Form FDA 483-item #10]

7. The IRB has failed to maintain a copy of a study protocol reviewed by the IRB.

8. The IRB's minutes of meetings do not adequately document the attendance at the meetings and the vote on IRB actions. [Form FDA 483-items #3 and #4]

9. The IRB has failed to obtain and document the information described in 21 CFR 56.115(a)(5) for each of the IRB members. [Form FDA 483-item #7]

Summary of Informed Consent Violations [21 CFR 50.20, 50.25(a)(1)(2)(3)(4)(5)(6)(7) and (8)]

10. The following statements pertain to the consent form approved by the IRB for the research study entitled: 

[REDACTED]
[REDACTED] [Protocol [REDACTED]].

- The last sentence in the informed consent document states, in part: "I . . . release Franklin Hospital Medical Center and the attending physician from liability for any results that may occur . . ." Since this statement appears to release the named parties from liability for negligence, it is exculpatory within the meaning of 21 CFR 50.20.
- The informed consent document lacks a statement that the study involves research, the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental. [Form FDA 483-item #2.a. and b.]
- The informed consent document lacks a description of any reasonably foreseeable risks or discomforts to the subject. [Form FDA 483-item #2.c.]
- The informed consent lacks a description of any benefits to the subject or to others which may reasonably be expected from the research. [Form FDA 483-item #2.c.]
- The informed consent lacks a disclosure of appropriate alternate procedures or courses of treatment, if any, that might be advantageous to the subject. [Form FDA 483-item #2.d.]
- The informed consent lacks 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 Food and Drug Administration may inspect the records. [Form FDA 483-item #2.e.]
- The informed consent lacks an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained. [Form FDA 483-item #2.f.]
- The informed consent lacks an explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of a research-related injury to the subject. [Form FDA 483-item #2.g.]
- The informed consent document lacks a statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

The above cited violations may not be all inclusive of the deficiencies in your IRB operation.

Administrative Restrictions

We have no assurance that your 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);*

- *no new studies that are subject to Parts 50 and 56 of the FDA regulations are to be approved by your IRB, and*
- *no new subjects are to be admitted to ongoing studies that are subject to 21 CFR Parts 50 and 56 until you have received notification from this office that adequate corrections have been made.*

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 IRB into compliance with FDA requirements. 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.

If you have any questions please contact Ms. Mary Jo Zollo at (301) 594-1026, Fax: (301) 594-1204. Your written response should be addressed to:

Mary Jo Zollo, Acting Team Leader
Human Subject Protection Team, (HFD-343)
Division of Scientific Investigations
Center for Drug Evaluation and Research
7520 Standish Place
Rockville, MD 20855

Sincerely yours,



David A. Lepay, M.D., Ph.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research

ENCLOSURE
Form FDA 483