DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

WARNING LETTER

APR 14 1998

OVERNIGHT MAIL

Ref. No. : 98-HFD-340-0401

Linda Janczak
President and CEO
F.F. Thompson Healthcare Systems, Inc.
350 Parrish Street
Canandaigua, New York 14424

Dear Ms. Janczak:

On February 2, 3 and 4, 1998, Steven J. Libal, an investigator with the Buffalo District Office of the Food and Drug Administration (FDA), conducted an inspection of the F.F. Thompson Hospital Institutional Review Board (IRB). 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. Libal issued a Form FDA 483 [enclosed] to Carol Dwyer, Vice President, Clinical Services, F.F. Thompson Healthcare Systems, Inc., which described the deviations from requirements specified under 21 CFR Part 50 and 56 that he had identified during the inspection. Mr. Libal also discussed these observed deficiencies with Robert Locke, R.Ph., IRB Secretary.

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. Libal's inspection report and the objectionable conditions and practices listed in the current Form FDA 483. The evidence shows that the IRB has failed to adhere to pertinent federal regulations as contained in 21 CFR 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) and (b)(1)]:

1. The IRB has failed to develop written procedures for conducting 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]

Summary of IRB Continuing Review Violation [21 CFR 56.109(f)]

3. The IRB has failed to conduct continuing review of ongoing research. [Form FDA-item #4]

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

4. 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 #2].

5. The IRB has failed to adequately document the vote on IRB actions in the minutes of IRB meetings [Form FDA 483-item #3].

6. The IRB has failed to maintain copies of records of continuing review activities, progress reports and a copy of a study protocol and an informed consent reviewed by the IRB [Form FDA 483-items #4 and #5].

Summary of Informed Consent Violations [21 CFR 50.20, 50.25(a)(1)(7) and (8)]

7. The following statements pertain to the consent forms approved by the IRB for the research studies entitled: "A Randomized, Double Blind, Multicenter Study of Low-Dose Gallium Nitrate for Treatment of Bone Metastasis Due to Breast Cancer" [Protocol # G5195] and "A Clinical Trial of Intravenous Navelbine for First Line Treatment of Women 60 Years of Age or Older with Advanced Breast Cancer" [Protocol # G2195].

- The informed consent document for Study Protocol #G5195 lacks a statement that the purpose of the research is to obtain safety data.

- The informed consent documents for Study Protocols #G5195 and #G2195 fail to include a person or office to contact in the event of a research-related injury to the subject.

- The informed consent documents for Study Protocols #G5195 and #G2195 fail to allow subjects to drop from the research without penalty. Both include statements that data will continue to be collected on subjects after withdrawal. The informed consent

- document for Study Protocol #G2195 also includes a statement that periodic tests will continue to be performed on subjects after withdrawal.

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
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