



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

WARNING LETTER

AUG 14 1998

Gary Goldstein, M.D.
Chief Executive Officer
Ochsner Foundation
1516 Jefferson Highway
New Orleans, Louisiana 70121

Dear Dr. Goldstein:

During the periods of February 18-26, 1997, and October 22-November 21, 1997, Biomedical Research Facility, a nonclinical laboratory facility of Alton Ochsner Medical Foundation, was visited by Rebecca A. Asente, Henry E. Sanchez, and Renee W. Bagneris, investigators with the Food and Drug Administration's (FDA) New Orleans District Office. The purpose of the inspectional visits was to determine whether your laboratory's activities and procedures complied with applicable FDA regulations.

The visits focused on the following nonclinical studies:



Our review of the information from the inspection reports submitted by the New Orleans District Office revealed violations of Title 21, Code of Federal Regulations (21 CFR) Part 58 - Good Laboratory Practices for Nonclinical Laboratory Studies. These findings were listed on the Form

FDA-483, Inspectional Observations (see enclosed copies). The FDA-483s were presented to and discussed with the Vice President and Research Director of Alton Ochsner Medical Foundation, Dr. Richard N. Re, at the conclusion of each inspection. The following list of violations is not intended to be an all-inclusive list of deficiencies observed during the inspections.

1. Failure to establish a Quality Assurance Unit to monitor each nonclinical study and to assure that the facilities, equipment, personnel, methods, practices, records, and controls are in conformance with applicable regulations as required in 21 CFR 58.29(b), 58.31, and 58.35.

The testing facility management failed to assure that:

- the facility has an impartial and independent Quality Assurance Unit (QAU);
- test articles, study documents, raw data, and specimens are maintained in accordance with 21 CFR 58.190;
- all study personnel are knowledgeable of their responsibilities;
- deviations from these regulations were corrected and documentation of the corrections was maintained and;
- final study reports for studies conducted before September 30, 1997, accurately described the methods and results.

The testing facility management failed to assure that the personnel followed the current written standard operating procedures entitled, "Alton Ochsner Medical Foundation Biomedical Research Standard Operating Procedures," dated September 30, 1997. For example, in Study [REDACTED] the testing facility failed to have current training summaries for each person involved in the study and documentation defining the critical phases and associated QAU audit schedule. Also, QAU did not control the receipt, storage, use or disposition of the test articles as required by these procedures.

The QAU did not maintain a complete and accurate master schedule of preclinical studies. The master schedule does not provide a list of all preclinical studies (current or historical), identify test articles, describe the studies performed, provide dates of study origination or closure, describe current study activity, or identify the study sponsors.

2. Failure to prepare written standard operating procedures (SOPs) as required by 21 CFR 58.81.

There were no written procedures available for the receipt, security, storage, maintenance, disposition, or inventory control of test articles; for laboratory tests, such as blood chemistry, urinalysis, and histological analysis; for specimen collection and labeling requirements; for histopathology; and for specimen archiving.

In addition, there were no written procedures requiring the submission of status reports to the testing facility management that would include problem reporting and corrective actions. In cases where current SOPs were available, there was no historical record of revisions to procedures developed before September 30, 1997.

3. Failure to have protocols that clearly define study objectives and methods as required by 21 CFR 58.120.

For example, the protocol for Study [REDACTED] did not fully describe the experimental design that included the methods for the control of bias. Also, the study protocol failed to: specify the frequency of tests, analyses, and measurements to be made; provide an exact description of the test system [REDACTED]; describe and/or identify the diet of the test systems; specify the records, including raw data collected, to be maintained; identify the name of the sponsor; and completely identify the test and control articles.

We also noted that written documentation of approval of protocols or revisions was inadequate for Studies [REDACTED]

[REDACTED]

4. Failure to conduct the study as required by 21 CFR 58.130.

For studies [REDACTED], the facility had no record of monitoring test systems for compliance with the protocols.

Study [REDACTED] was not conducted in accordance with the study protocol.

[REDACTED]

Specimens were not identified in a manner to preclude error in the recording of data. For example, specimens from Study [REDACTED] were labeled [REDACTED] with no other information to correlate specimens to test systems.

All data generated during the conduct of these nonclinical laboratory studies were not prepared and documented as required by this regulation. In Study [REDACTED] inappropriate changes were noted in data entries, such as obscuring entries in animal care charts and other records. The reasons for these changes were not documented. Also, some records associated with the study were not dated and signed by the person responsible for direct data input.

5. Failure to maintain study documentation and to store material in an orderly fashion for expedient retrieval as required by 21 CFR 58.190.

For the above referenced studies, documentation was either not retained or not readily retrievable for approved protocols, specimens, raw data, and final reports.

For example, in Study [REDACTED] the raw data [REDACTED]

[REDACTED] to verify the

data's existence. Additionally, [REDACTED] data were unavailable for all test systems in the study.

The records documenting the calibration and maintenance of the equipment used in study [REDACTED] were not adequate. There was no documentation available for [REDACTED] used in the study and whether the [REDACTED] was calibrated as scheduled [REDACTED]. Records indicated that the [REDACTED] was last calibrated in 1990. Also, documentation identifying the hardware and software used in the study was not available. A journal article was the sole documentation of equipment validation for [REDACTED] used in the study.

The records of the studies, [REDACTED]

[REDACTED] were incomplete, and the final reports were not prepared in accordance with 21 CFR 58.185.

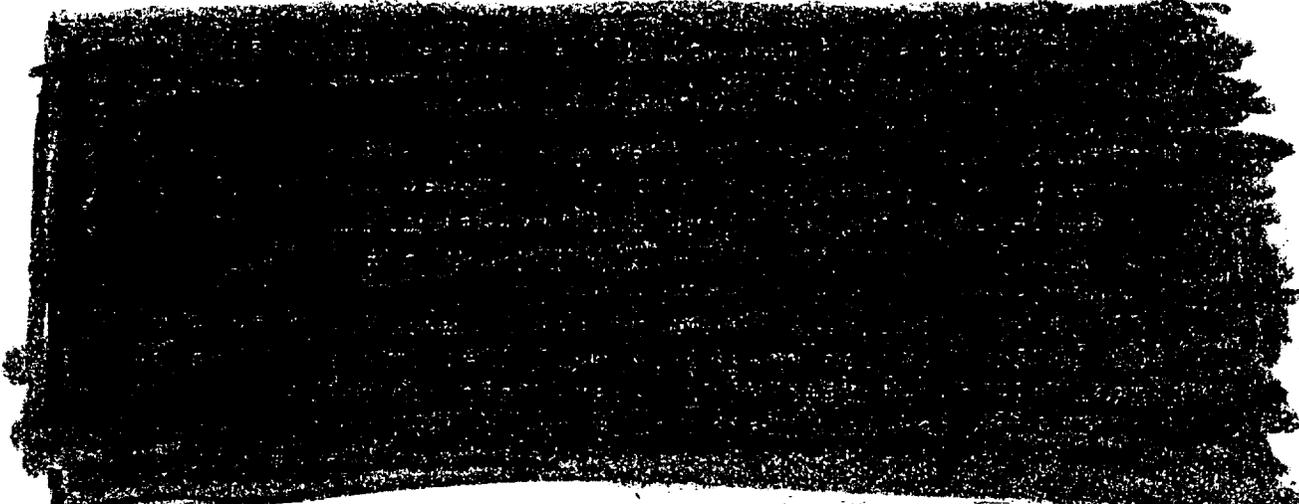
Dr. Re's March 17, 1997, letter responded to the Form FDA-483 issued on February 26, 1997. This response attempts to address issues related specifically to the nonclinical studies. [REDACTED]

However, for other studies covered, observations associated with the above referenced violations were not addressed.

[REDACTED] studies that were the subject of FDA's inspections at your facility were submitted in support of applications for research or marketing permits of products regulated by the FDA. With the exception of Studies [REDACTED] which are on-going, the nonclinical data submitted in these applications were incorrectly represented to the FDA as having been collected in compliance with the Good Laboratory Practices for Nonclinical Laboratory Studies regulations, 21 CFR part 58.

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The nature and severity of your deviations from the GLP regulations seriously compromise the reliability of the nonclinical laboratory studies. As a result, in accordance with 21 CFR 58.215(b), we are recommending to the appropriate Divisions within FDA's Office of Device Evaluation, that they refuse to consider the following safety studies received in support of research or marketing permits that were conducted by your testing facility:



This letter is notification that the GLP deficiencies observed during this inspection be corrected before any nonclinical laboratory studies intended for submission to FDA are planned, begun, or continued. It is your responsibility to implement a corrective action plan that addresses these deficiencies and provides for correction in on-going and future studies. We have advised the New Orleans District Office of these actions and will request them to perform a reinspection of your facility after you have made corrections. We recommend that you inform the District Office of your corrective action timetable:

Further, all prior studies conducted by this facility to support research or market applications submitted to FDA must be identified by providing a master schedule to this office of all nonclinical studies conducted at this facility and required to be maintained by 21 CFR 58.35(b)(1). Additionally, you must notify each sponsor that their studies were not conducted in accordance with the GLP regulations. A copy of this notification must also be sent to our office.

In addition to the above, you must notify this office, in writing, within fifteen (15) working days of receipt of this letter, of the specific corrective actions you have taken,

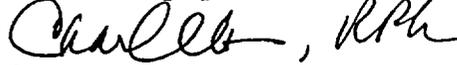
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or will be taking, to correct these deficiencies and to achieve compliance with FDA regulations. These actions should include the development and implementation of new and revised nonclinical laboratory policies and procedures. If you are unable to respond within 15 working days, you may request an extension by stating the reason for the delay and the time within which you expect your response to be completed. Failure to take prompt action to correct these deficiencies may result in further regulatory action including disqualification of the facility.

Please direct your response to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, Program Enforcement Branch I (HFZ-311), 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kevin M. Hopson. We also request that you send a copy of your response to the FDA New Orleans District Office, 4298 Elysian Fields Avenue, New Orleans, Louisiana 70122.

If you have any questions concerning this matter, please contact Mr. Kevin Hopson at (301) 594-4720, extension #128.

Sincerely yours,

for 

Lillian J. Gill
Director
Office of Compliance
Center for Devices
and Radiological Health

Enclosures

cc: George Porter, M.D.
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