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Via Federal Express

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

FEB 14 2003

WARNING LETTER

David Skaggs, M.D.
Children's Hospital, Los Angeles
4650 Sunset Boulevard (Mailstop #88)
Los Angeles, California 90027-6062

Dear Dr. Skaggs:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection conducted at your clinical site and to request a prompt reply. Mr. Allen Hall, an investigator from the FDA's Los Angeles District Office, conducted the inspection at your site from November 5 through 7, 2002. While you were interviewed during portions of the inspection, you directed our investigator to Cheryl S. Lew, M.D., Interim Principal Investigator, and her staff for inspectional responses.

The purpose of the inspection was to determine if your activities and procedures as a clinical investigator for the [REDACTED] study for use in a pediatric population, sponsored by [REDACTED], complied with applicable regulations. The [REDACTED] is a device as that term is defined under Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C.321(h)].

This inspection was conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemptions (IDE), Premarket Approval (PMA), and Premarket Notification [510(k)] submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report prepared by the Los Angeles District Office reveals violations of requirements of Title 21, Code of Federal Regulations (21 CFR), Part 50 - Protection of Human Subjects and Part 812 - Investigational Device Exemptions. At the conclusion of the inspection, Mr. Hall listed his findings on a Form FDA 483, "Inspectional Observations," and discussed these findings with Dr. [REDACTED]. We note that the [REDACTED] Committee on Clinical Investigations (IRB) suspended your participation in this study until further notice.

This letter informs you of the violations found during our inspection and our subsequent review of the inspection report. The following violations were observed:

Failure to document the informed consent by use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. 21 CFR 50.27(a); 812.100; and 812.140(a)(3)(i).

Two subjects had their surgery performed before written informed consent was documented for these subjects (subjects # [REDACTED] and # [REDACTED]). Both subjects underwent surgery on [REDACTED] and written informed consents were obtained on [REDACTED] and [REDACTED] respectively.

FDA regulations require that information provided to study subjects or representatives is in language understandable to the subject or the representative. 21 CFR 50.20. The informed consent forms in this study were provided in English. Two of the subjects' parents (subjects # [REDACTED] and # [REDACTED]), who were their legal representatives, spoke a foreign language and required translation. Informed consent may therefore not have been adequately provided.

Failure to ensure that the investigation is conducted according to the signed agreement with the sponsor and the investigational plan, 21 CFR 812.100, and failure to maintain accurate records of each subject's case history and exposure to the study device, including supporting data and medical records, 21 CFR 812.140(a)(3).

Case report forms (CRFs) were not completed in a timely manner for numerous subjects, physical examinations were not completed or were not documented, and required examinations (CT and Echo) were not performed as required by the protocol. These deficiencies were evident in the CRFs for subjects # [REDACTED], # [REDACTED], and # [REDACTED].

As a clinical investigator, it is your responsibility to ensure that investigations in which you participate are conducted in accordance with applicable FDA regulations. In response to several of the observations made during the FDA inspection, you stated that you had limited staff resources and had difficulty maintaining the study records. Failure to adequately adhere to informed consent requirements can adversely affect the subjects enrolled in a study. Failure to adhere to the investigator's agreement and the established protocol can also adversely affect subjects enrolled in the study, the results obtained, and the site's credibility, and may ultimately discredit the entire study. If adequate resources to comply with applicable requirements are not available, you and the sponsor of a study should not proceed with the study. This determination should be made early in the process of selecting potential investigators and is the responsibility of the investigator, monitor, and the sponsor of the study.

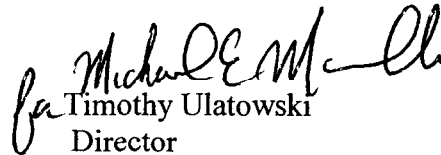
Please advise this office, in writing, **within fifteen (15) working days of receipt of this letter** of the additional specific steps you have taken to correct these violations and to prevent the recurrence of similar violations in current or future studies. Failure to respond can result in the initiation of regulatory action, including disqualification, without further notice.

You should direct your response to the following address:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Program Enforcement Branch II, (HFZ-312)
2098 Gaither Road
Rockville, Maryland 20850
Attention: Mr. G. Levering Keely, BSN, MPA,
Consumer Safety Officer.

A copy of this letter has been sent to our Los Angeles District Office, 19900 MacArthur Blvd., Suite 300, Irvine, CA 92612. We request that a copy of your response be sent to that office as well.

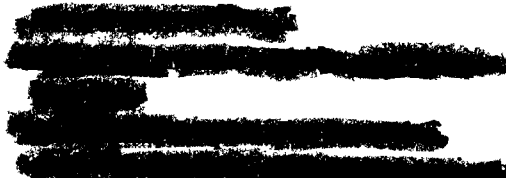
Sincerely yours,


Timothy Ulatowski

Director
Office of Compliance
Center for Devices and
Radiological Health

Purged Copies to:

IRB


Institutional Review Board
