



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

FOI request
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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG - 6 1999

WARNING LETTER

Federal Express

Abdool R. Moossa, M.D.
Chairman, Surgery Department
University of Southern California
402 Dickinson Street, Suite 260
San Diego, California 92103

Dear Dr. Moossa:

During the period of May 21 through June 9, 1999, Mr. Allen F. Hall, an investigator with the Food and Drug Administration's (FDA) Los Angeles District Office, visited you, Rachel Ramiro, and Theresa Barnett. The purpose of that visit was to conduct an inspection to determine whether activities and procedures associated with the investigational study of the [REDACTED] [REDACTED] complied with applicable FDA regulations. This product is a device as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval Applications (PMA), and Premarket Notifications [510(k)] 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 submitted by the district office revealed that there were significant violations of Title 21, Code of Federal Regulations (21CFR), Part 812 – Investigational Device Exemptions and Part 50 – Informed Consent of Human Subjects. At the conclusion of the inspection, Mr. Hall issued a Form FDA-483, "Inspectional Observations" to you, which described the deficiencies identified during the inspection. Also present were [REDACTED]. The following list of violations is not intended to be an all-inclusive list of deficiencies in the above referenced clinical study.

1. **Failure to obtain and provide informed consent in accordance with 21 CFR 50.20.**
 - a) Someone signed informed consent documents for [REDACTED] and [REDACTED]. There was no documentation to show that the individuals signing the consents were the authorized legal representatives for the subjects.
 - b) Informed consent documents used for [REDACTED] were not in a language understandable to the subjects. The informed consent document states that an interpreter was used. The contract research organization representative requested an explanation of this procedure and requested that you report this deviation to the IRB. You reported to the IRB; however, information on [REDACTED] was not included in the report.

It is the responsibility of the investigator to ensure that informed consent is obtained in accordance with FDA regulations for the Protection of Human Subjects and that a copy of the signed form is given to the person signing the form. This includes providing the study subject with an informed consent that is in a language that is understandable to the subject.

Furthermore, investigators may not involve a human being as a subject in research unless the investigator has obtained informed consent of the subject or the subject's legally authorized representative.

2. **Failure to prepare and submit complete, accurate, and timely reports to the sponsor and to the reviewing IRB as required by 21 CFR 812.150(a)(1) and (3).**
 - a) Adverse effects for [REDACTED] were reported 3 months after the event. Adverse effects for subjects [REDACTED] were reported to the IRB approximately 9 months after the event and to the sponsor approximately 5 months after the event. The IRB required a written report of unexpected events no later than 10 working days after the event.
 - b) The progress report dated 9/24/98, and submitted to the reviewing IRB, erroneously states that there was a Data Safety Monitoring Board for the study. We acknowledge that this was due to a misunderstanding and that you corrected this information with the IRB.

Investigators are required to prepare and submit complete, accurate, and timely reports to the sponsor and reviewing IRB of any unanticipated adverse effect occurring during the investigation. In addition, accurate progress reports are to be submitted to the sponsor and the IRB.

3. Failure to conduct an investigation in accordance with the investigational plan (21CFR Part 812.110(b)).

You failed to follow the protocol in that:

- a) [REDACTED] was used for [REDACTED]. Section 7.3.2.1 of the protocol states that "The addition of [REDACTED] is prohibited for purposes of this study."
- b) Post-surgery laboratory specimens were not collected for [REDACTED]. The protocol required that they be collected at 2-4 weeks and 4-6 weeks after surgery.
- c) Preoperative laboratory specimens were not collected for [REDACTED].
- d) Randomization procedures were not followed. Randomization envelope [REDACTED] was not returned for use with the next subject. The study dispensing form indicates that the envelope was dispensed 2/26/98 and not used.
- e) Subject randomization envelopes and study devices for subjects [REDACTED] were incorrectly allotted to subjects who did not receive orthopedic surgeries.

In addition to the above, it was noted that you enlisted and released the study device to physicians who had not signed an investigator's agreement and had not been identified to the IRB as co-investigators. As the principal investigator, you should not supply the device to any person not authorized to receive it and the device should only be used with subjects under your supervision [21 CFR 812.110(c)].

It is your responsibility, as a clinical investigator, to ensure that your investigation is conducted in accordance with the signed agreement with the sponsor, the investigational plan, and applicable FDA regulations.

Please advise this office, in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct these violations and to prevent recurrence of similar violations in current or future studies. Your failure to respond may result in further regulatory action, without notice, including disqualification. Please send your response to the 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: Pamela M. Reynolds. A copy of this letter has been forwarded to our Los Angeles District Office, 19900 MacArthur Blvd, Suite 300, Irvine, California 92612. We request that a copy of your response be sent to that office.

If you have any questions or concerns, feel free to contact Pamela Reynolds at (301) 594-4720, extension 155.

Sincerely yours,



for

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