DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

M3971

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

WARNING LETTER

JUL 18 2000 ***Via Federal Express***

Michael R. Rose, M.D.
South Coast Eye Institute
3420 Bristol Street, Suite 700
Costa Mesa, California 92626

Dear Dr. Rose:

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. The inspection took place during the period of March 27 and May 4, 2000, and was conducted by Ms. Suzie L. Kent, an investigator from FDA's Los Angeles District Office. The purpose of the inspection was to determine the present location of the investigational [redacted] you used in studies sponsored by [redacted] and under your own independent Investigational Device Exemption (IDE). Another purpose of the inspection was to determine if your activities as a clinical investigator with this [redacted] comply with applicable FDA regulations. [redacted] are devices 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 serious violations of requirements of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions, Part 50 - Protection of Human Subjects, and Section 520(g) of the Act. The deviations noted were listed on a form FDA-483, "Inspectional Observations," which was issued at the conclusion of the inspection and discussed with you. Deviations noted include the following:

Failure to properly supervise and dispose of an investigational device [21 CFR 812.110(c) and (e)].
The investigational [redacted] was transferred to a third party not authorized to receive it and was not disposed of as directed by the sponsor.

Failure to submit progress and final reports to the reviewing institutional review board (IRB) and the sponsor [21 CFR 812.150(a)(3) and (6)].
Despite reminder letters from Clinical Review Associates, the reviewing IRB, and from [redacted] no progress reports were submitted during the investigation. Moreover, no final report was submitted at the termination of the study. The obligation to submit these reports is included in the study protocol. Therefore, lack of these reports is also a failure to follow the investigational plan, a violation of 21 CFR 812.100 and 110(b).

Failure to use the IRB-approved informed consent document for study subjects [21 CFR 50.27(a)].
The consent form used during the study did not contain the requirement that female subjects be administered pregnancy tests as specified by the IRB. Moreover, at least one subject received a monetary incentive to keep a follow-up appointment. Monetary incentives were not approved by the IRB for this study.

Failure to follow the investigational plan [21 CFR 812.100 and 812.110(b)].
At least one subject having a condition listed among the exclusion criteria was included in the study, with no documentation of the reasons for inclusion. Moreover, there is no documentation that corrective actions taken to prevent shifts in output alignment were successful before the treatment of subjects.

Failure to maintain accurate subject records [21 CFR 812.140(a)(3)].
Evaluation reports for the 12-month and 18-month follow-ups of a study subject were present in duplicate, with conflicting information.

The deviations listed above are not intended to be an all-inclusive list of deficiencies that may exist in your clinical study. It is your responsibility as a clinical investigator to ensure that an investigation is conducted according to the signed agreement, the investigational plan, and applicable FDA regulations.

The inspection report also notes that Ms. Kent discussed several issues with you that were not included on the form FDA-483. These include:

- Changes and corrections were made without initials or explanation.
- There is no documentation of [redacted] calibrations and checks.
- There is no documentation of the variable [redacted] output problems that you state resulted in your termination of participation in the study.

The report also states that you are no longer participating in clinical trials.

Please acknowledge receipt of this letter within 15 working days, stating what corrective actions you would initiate if you were to consider participation in future clinical trials. One way to control the conduct of studies at your site is the

development of standard operating procedures (SOPs). These SOPs would include directions for personnel responsible for the informed consent process that include the following: a method for assuring that the inclusion/exclusion criteria for the study are observed; that potential subjects are fully aware of what is expected of them and willing to commit to the study requirements; and that accurate and complete documentation of the process is maintained, as evidenced by dates and signatures on the IRB-approved informed consent document. SOPs would also include procedures for verification of data entered on case report forms (CRFs) and specify responsible personnel. They should also delineate the required interactions with the reviewing IRB, as well as methods of device accountability. This is not necessarily a complete listing of the contents of clinical study SOPs.

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: Jean Toth-Allen, Ph.D. Failure to respond could result in further regulatory action without additional notice, including initiation of investigator disqualification procedures.

A copy of this letter has been sent to FDA's Los Angeles District Office, 19900 MacArthur Boulevard, Suite 300, Irvine, California 92715. We request that a copy of your response also be sent to that office.

If you have any questions, feel free to contact Jean Toth-Allen, Ph.D. at (301) 594-4723, ext. 141.

Sincerely yours,

Steven M. Niedelman
Acting Director
Office of Compliance
Center for Devices and Radiological Health

cc:

[redacted] (purged copy)

James H. Stallings, Jr. M.D., F.A.A.P. (purged copy)
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