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Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUN 15 2000

WARNING LETTER
*Via Federal Express*John R. Wright, D.O.
Wright Eye Center
2920 North Cascade Avenue
Colorado Springs, Colorado 80907

Dear Dr. Wright:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a Food and Drug Administration (FDA) inspection of your clinical site, to discuss your response to the findings, and to request a prompt reply. The inspection took place during the period of March 27 and April 10, 2000, and was conducted by Ms. Patricia Cortez, an investigator from FDA's Denver District Office. The purpose of the inspection was to determine if your activities as a clinical investigator of [REDACTED] comply with applicable FDA regulations. This system 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 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. You received a form FDA-483, "Inspectional Observations," at the conclusion of the inspection that listed the deviations noted and discussed with you. We acknowledge receipt of a copy of your response to the Director of the Denver District Office dated May 3, 2000. The deviations noted include:

Failure to ensure that an investigation is conducted according to the investigational plan [21 CFR 812.100 and 812.110(b)].

Various protocol violations were noted including:

- 11 out of 25 study subjects either did not meet all inclusion criteria or were not fully evaluated against the criteria prior to enrollment in the study.

- 11 of the 25 subjects did not sign the informed consent document prior to scheduling surgery.
- There was no record that regular progress reports were made to the sponsor.
- An independent laboratory was not used to conduct the corneal endothelial cell count.
- You did not record measurements for all required tests for all visits.
- 13 of the 25 subjects did not have at least one follow-up visit during the prescribed timeframe.
- Documentation of treatment parameters for the device was missing on 6 of the 25 subject records.
- Case report forms (CRFs) for the preoperative evaluation were not sent to the monitor within 5 business days for at least 9 of the 25 subjects.
- An unsigned informed consent document was sent to the monitor resulting in an extra subject counted as part of the study when the individual later chose not to participate.
- The Monitor did not receive the original certification of institutional review board (IRB) approval.
- The version of the protocol at the site was not the most recent version.

Failure to maintain complete and accurate subject records [21 CFR 812.140(a)(3)].

You were unable to locate the case history records for one of the study subjects during the time of the inspection. The records for 3 study subjects contained multiple CRFs for the same, with conflicting information. Moreover, you did not record all observations related to the condition of the subjects and the progress of the procedure on the CRFs.

Failure to maintain all records of correspondence with the sponsor [21 CFR 812.140(a)(1)].

You failed to document interactions with the sponsor regarding the protocol. In particular, you did not have documentation that the sponsor agreed to use of your internal laboratory for the corneal endothelial cell count.

Failure to report a protocol deviation to the reviewing IRB [21 CFR 812.150(a)(4)].

In two cases you reverted to use of the ultrasound equipment to completely emulsify

the cataractic lens, though the procedure was started with the investigational laser. While not necessarily an emergency procedure, to change devices in mid-procedure indicates that the original device was not producing satisfactory results. Therefore, the change was made for the good of the subject. Moreover, it was a deviation from the protocol. This should have been reported to both the sponsor and the IRB, at least in a progress report if not sooner.

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 first several pages of your response discuss those observations noted in the subject records but not on the CRFs and which were listed as unreported adverse effects on the form FDA-483. Your response notes that several of the observations in the charts were not related to the surgery. It is the responsibility of an investigator to report all procedural events and medical conditions and/or changes noted in a subject during the course of the study that would not have been expected to occur. Those not related to the device or procedure used will be obvious to the sponsor, as they will be singular events. However, if similar findings should be noted for several subjects and by several investigators, an unanticipated effect or procedural complication may become obvious when all records are reviewed.

Your response notes that you were not aware that you should be maintaining a record of interactions with the sponsor that included a phone log of conversations. You also state that you received a letter from [REDACTED] allowing you to take your own endothelial cell counts. The inspectional report notes that you stated during the inspection that this permission was given on the phone. In either case, you did not present documentation during the inspection nor did you include any with your response.

Item 11 on the form FDA-483 notes that informed consents were not sent to the monitor within the 5 days stipulated in the protocol. Your response states that they were, though the dates noted for signing and sending are more than 5 days apart. Moreover, you state that it is "a violation of patient confidentiality and breaches our medical/legal responsibility to keep the original informed consents in our office for items #11 A-H." This statement is confusing as to its relevance regarding the finding of late transmission of information. Moreover, it would be expected that all patient information be routinely maintained in patient files at a doctor's office. Please explain this statement.

You state that the Study Coordinator inadvertently filled out 2 one-week post op forms for several subjects. That does not explain the inconsistencies between the forms, even if some terms have the same meaning. Moreover, it is the responsibility of the investigator to review and sign subject case report forms before they are made a permanent part of the record.

With regard to missing endothelial cell count information, you state that some procedures were forgotten and that poor development was the fault of the photo lab. It is your responsibility as the investigator to assure all required measurements are taken. You are also responsible for choosing qualified laboratories to process your results.

It is the responsibility of the investigator to assure that potential subjects are fully advised of the study expectations as part of the informed consent process. When study subjects do not meet the required follow-up schedule, the data is not useable for support of a submission for marketing. When the sponsor is unable to include a subject's results in the analysis of the study, the subject has received an investigational device and/or procedure, putting them at greater risk than conventional treatment, with no potential benefit to anyone.

According to the inspectional report, [REDACTED] has requested that you begin enrolling subjects again. Please inform us of the corrective actions you have taken to assure that the study is conducted according to the investigational plan and the pertinent regulations. Please send all the information requested, within 15 working days of receipt of this letter, 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 Denver District Office, Denver Federal Center, Building 20, 6th Avenue and Kipling Street, Denver, Colorado 80225. 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,



for

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

cc:

[REDACTED] (purged copy)
Chairman and CEO

[REDACTED]
[REDACTED]
[REDACTED]

William Lloyd, M.D., Chair (purged copy)
The Institutional Review Board
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