



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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FEDERAL EXPRESS

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Food and Drug Administration
Rockville MD 20857

WARNING LETTER

Robert W. Schaefer
President/CEO
Apple Medical Corporation
580 Main Street
Bolton, Massachusetts 01740

Dear Mr. Schaefer:

During August 26 through September 8, 1997, Sandra P. White, an investigator with the U.S. Food and Drug Administration (FDA), New England District Office, visited your facility. The purpose of that inspectional visit was to determine whether the activities of the [REDACTED] a division of Apple Medical Corporation, as the Sponsor of the investigational study of the [REDACTED] [REDACTED] complied with applicable FDA regulations. This product is a device as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act.

Our review of the inspection report, as well as the inspection reports for the May 1997 audits of participating clinical investigators (Drs. [REDACTED])

revealed violations of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions. The findings from your inspection were listed on form FDA-483, Inspectional Observations, which was presented to and discussed with you at the conclusion of the inspection.

The following list of violations is not intended to be an all-inclusive list of the problems encountered during our reviews. We have listed FDA's inspectional findings related to deficiencies in your role as the sponsor of the referenced investigational device study so that you may correct your study monitoring procedures.

- (1) Failure to ensure proper monitoring of the clinical investigation as required in 21 CFR 812.40.

Although you developed written procedures for monitoring the investigational study entitled, "Clinical Monitoring Standard Operating Procedure, [REDACTED] Sponsored Studies," dated October 11, 1995, there were no documents available to determine how you assured the selection of a qualified monitor. There were no formal written agreements between you and [REDACTED] your contract monitor, to determine the extent of their responsibilities.

Monitoring visits were conducted by you and [REDACTED] during the clinical investigation. However, the monitoring was inadequate in that there was a failure by the monitor to identify problems which included under-reporting of adverse events, informed consent deficiencies, and protocol deviations.

For example, subject informed consent documents were incomplete at two of the three clinical sites (Drs. [REDACTED] and device accountability records were inadequate at all sites. Incomplete records of patient histories and device prescription registration forms were not identified by, or reconciled as a result of, the monitoring visits.

Review of subject records disclosed that some adverse events and complications were not reported to the Sponsor, [REDACTED] or the responsible Institutional Review Boards (IRB). Consequently, these events were not properly reported to FDA in the associated Pre-Market Notification application [510(k)].

(2) Failure to ensure investigator compliance as required by 21 CFR 812.46.

Violations of the regulations were found at each of the clinical investigator sites including: failure to maintain accurate, current, and complete study records; failure to maintain adequate device accountability; failure to obtain proper informed consent; deviations from the study protocol, and failure to report those deviations to their respective IRBs.

[REDACTED] did not institute actions during the study to achieve investigator compliance. In fact, two of the three participating investigators, Drs. [REDACTED] and [REDACTED] failed to obtain IRB approval for the study protocol and informed consent document, prior to initiating the study. As a result of this, and other compliance problems, FDA issued warning letters to Dr. [REDACTED] (December 23, 1997), Dr. [REDACTED] (October 14, 1997), and Dr. [REDACTED] (October 2, 1997).

- (3) Failure to label the investigational devices per the requirements of 21 CFR 812.5(a).

Labeling which included the following required statement: "CAUTION- Investigational device. Limited by Federal (or United States) law to investigational use" was not affixed to the devices or their immediate packaging.

- (4) Promotion of an investigational device in a manner prohibited by 21 CFR 812.7(d).

The ordering instructions provided to the subjects did not contain any statements that the device was investigational. Furthermore, those instructions inappropriately suggested that the investigational device was effective for the treatment for [REDACTED].

Also, you advertised the [REDACTED] in The Boston Globe, The New York Times, and The Richmond Dispatch newspapers as a new technology. The advertisements failed to identify the device as investigational, hence these advertisements misrepresent the device as safe and effective for the purposes for which it is being investigated.

- (5) Failure to provide accurate, complete, and current information as required by 21 CFR 812.150(b).

Our review of your records indicated that FDA was not notified about the termination of [REDACTED] as a study monitor. Also you did not submit progress reports to any of the three reviewing IRBs.

Information in the 510(k) submission to FDA indicated that [REDACTED] was not permitted. However, the device package insert contradicts the protocol and the physician instruction pamphlet because it describes [REDACTED] as an option for the study subjects.

Our audit of Dr. [REDACTED]'s study records disclosed that a "fact sheet" provided by the sponsor listed [REDACTED] an option for study subjects. No documents were available to indicate that you or the contract monitor took corrective actions to cease [REDACTED]

While none of the previously listed violations prevented the eventual clearance of your premarket notification, it is your responsibility to ensure adherence to each requirement of the Act and regulations. Within 15 days of receipt of this letter, please provide this office with written documentation of the specific steps you have taken to correct these violations and to prevent the recurrence of similar violations in current and future studies.

Your response should be directed to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 2098 Gaither Road, Rockville, Maryland 20850, Attention: Kevin M. Hopson. A copy of this letter has been sent to the Food and Drug Administration's New England District Office, One Montvale Avenue, Stoneham, Massachusetts 02180. We request that a copy of any correspondence from you also be sent to that office.

Should you require additional time to respond, or have any questions concerning this matter please contact Mr. Kevin Hopson at (301) 594-4720, ext. 128.

Sincerely yours,



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