



WARNING LETTER

Food and Drug Administration
Rockville MD 20857

DEC 30 1999

Via Federal Express

Mark D. Robinson
President
Medical Developmental Research, Inc.
2451 Enterprise Road
Clearwater, Florida 33763

Dear Mr. Robinson:

During the period of August 18-25, 1999, Mr. Michael Roosevelt and Ms. Christine Humphrey, investigators from the Food and Drug Administration's (FDA), Florida District Office, visited your firm. The purpose of that visit was to conduct an inspection to determine whether your firm's activities relating to 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 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 submitted by the district office revealed that there were deviations from the requirements of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions. These deviations were listed on the Form FDA 483, "Inspectional Observations," which was presented to and discussed with you at the conclusion of the inspection.

Failure to maintain records of shipment and disposition in accordance with 21 CFR 812.140(b)(2).

Medical Developmental Research, Inc. (MDR) failed to maintain records of shipment and disposition of devices including the name and address of consignee, type and quantity of device, date of shipment, and batch number or code mark. For example, two physicians implanted at least two devices in 1994, yet there were no records of the two implants in the firm's Monthly Implant Report. Sponsors are required to maintain device accountability records for all devices shipped, returned, or disposed of.

Failure to maintain control of the device according to 21 CFR 812.43(b).

MDR failed to maintain control of investigational devices in that they shipped devices to nine unauthorized investigators. A review of MDR's Monthly Implant Reports disclosed that MDR failed to obtain signed investigator agreements prior to shipping 44 investigational devices to nine investigators.

Failure to obtain signed investigator agreements in accordance with 21 CFR 812.43(c).

MDR failed to obtain signed written investigator agreements for each investigator participating in the study. A review of study documents disclosed that MDR did not have signed investigator agreements on file for nine of thirty-eight investigators participating in the [REDACTED]. Moreover, two investigators signed investigator agreements after implanting investigational devices. As a sponsor, you are required to obtain signed investigator agreements for each investigator participating in the study.

Failure to ensure proper monitoring of the study in accordance with 21 CFR 812.40.

MDR failed to monitor its [REDACTED]. According to Ms. Maylene Dunham, General Manager, there have been no site monitoring visits since the study began. We note that MDR sent letters to three investigators in 1994 and 1995 requesting investigator statements and *curricula vitae*. However, there was no other documentation of study monitoring noted during the inspection. As a sponsor of an investigational study, you are responsible for **ensuring proper monitoring of the study**, for selecting qualified investigators and providing them with information they need to conduct the investigation properly, ensuring that IRB review and approval are obtained, and ensuring that the reviewing IRB and FDA are promptly informed of significant new information about the investigation.

Failure to have written procedures for monitoring the investigation in accordance with 21 CFR 812.25(e).

MDR lacks written procedures for monitoring clinical studies. According to Ms. Dunham, MDR is not currently using any monitoring procedures, including those written by the previous owners of the firm, to monitor ongoing studies. Sponsors are required to have and follow written procedures for monitoring investigations including the names and addresses of any monitors.

Failure to maintain records of Institutional Review Board (IRB) approval in accordance with 21 CFR 812.140(b)(1).

MDR failed to maintain records documenting IRB approval for each investigational site participating in the study. Sponsors are required to maintain complete and accurate records regarding correspondence with another sponsor, a monitor, an investigator, an IRB, or FDA, including required reports.

Failure to submit reports to the FDA in accordance with 21 CFR 812.150(b)(1) and (5).

- MDR failed to submit reports of unanticipated adverse events to the FDA and to the reviewing IRB within ten working days after receiving notice of the events. For example, in June 1999, MDR received two complaints [REDACTED] concerning lenses that were explanted due to a film on the lens that resulted in subsequent reduction in patient vision. MDR did not report these incidents to the FDA. During the last inspection, it was observed that MDR had failed to establish a written Medical Device Reporting Procedure for submitting Medical Device Reports to the FDA. The current procedure fails to address how reportable events are to be submitted to the FDA.
- MDR has not submitted any progress reports to the FDA for at least 18 months. As a sponsor, you are required to submit progress reports to the FDA at regular intervals, at least yearly.

Failure to secure compliance in accordance with 21 CFR 812.46.

MDR failed to secure investigator compliance from at least 17 of 38 clinical investigators who did not submit case report forms (CRFs) for subjects receiving the investigational device. In addition, a review of CRFs for study subjects of the 21 clinical investigators who had documented CRFs on file revealed that there were no CRFs on file for at least 61 of 176 subjects. A sponsor who discovers that an investigator has not complied with the signed agreement, the investigational plan, or other applicable FDA regulations, or any condition of approval imposed by the IRB or FDA, shall promptly either secure compliance, or discontinue shipments of the device to the investigator and terminate the investigator's participation in the investigation.

The above deviations are not intended to be an all-inclusive list of deficiencies which may exist in your clinical study. It is your responsibility to assure adherence to each requirement of the Act and regulations.

We acknowledge your letter of August 25, 1999, to the Florida District Office in response to the inspectional observations in which you stated that the [REDACTED] [REDACTED] has been out of control due to employee turnover and to a facility move. We note that MDR submitted a supplement to its [REDACTED] to the Office of Device Evaluation requesting a ninety-day extension to submit its overdue annual progress report.

Within fifteen (15) working days of receipt of this letter, please provide, in writing, the specific steps you have taken to correct these violations and to prevent the recurrence of similar violations in current or future studies. You should direct 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, Attn: Robert Fish, Consumer Safety Officer. Your failure to respond may result in further regulatory action. A copy of this letter has been sent to our Florida District Office, 555 Winderley Place, Suite 200, Maitland, Florida 32751. We request that a copy of your response be sent to that office.

If you have any questions or require additional time to respond, you may contact Mr. Fish at (301) 594-4723, extension 138.

Sincerely yours,



for

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