



Via Federal Express

AUG 15 2005

WARNING LETTER

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

Mr. Michael Londo
Lifestream Medical Corporation
P.O. Box 517
Windermere, Florida 32786

Dear Mr. Londo:

The purpose of this Warning Letter is to inform you of objectionable conditions found during a recent Food and Drug Administration (FDA) inspection at your firm. This letter also requests that prompt corrective actions be implemented in response to the violations cited. The inspection took place during the period from April 21 through April 26, 2005, and was conducted by an investigator with FDA's Florida District Office.

The purpose of the inspection was to determine if your activities as a sponsor of human research studies complied with applicable FDA regulations, published in Title 21, Code of Federal Regulations (21 CFR), Part 50-Protection of Human Subjects, and Part 812-Investigator Device Exemptions. [REDACTED] manufactured by [REDACTED], is a device as that term is defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (Act) [21 U.S. C. 321(h)].

The inspection was conducted under a program designed to ensure that data and information contained in applications for Investigational Device Exemption (IDE), Premarket Approval (PMA) applications, 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 prepared by the Florida District Office revealed violations of 21 CFR Part 812 – Investigational Device Exemptions. The FDA investigator listed his findings on a Form FDA-483, "Inspectional Observations," and discussed these findings with you at the conclusion of the inspection.

The deviations noted in the FDA-483 and issues from the subsequent review of the inspection report are discussed below:

1. Failure to ship investigational devices only to qualified investigators participating in the investigation. [21 CFR 812.43(b)]

Pursuant to 21 CFR 812.43(b), a sponsor shall ship investigational devices only to qualified investigators participating in the investigation. Examples of this failure include but are not limited to the following:

You shipped investigational devices (components /replacement parts) to individuals who were not approved clinical investigators. From October 1999 to March 2005, you sent approximately 125 shipments of investigational devices directly to subjects.

- a. Subject [REDACTED] in [REDACTED] received [REDACTED] and [REDACTED] from you on the following dates: [REDACTED]
- b. Patient [REDACTED] (who is not a subject of this device study) in [REDACTED] received [REDACTED] on the following dates: [REDACTED] and [REDACTED]. This non-study patient also received an [REDACTED] on [REDACTED].
- c. Patient [REDACTED] (who is not a subject of this device study) in [REDACTED] received [REDACTED] on [REDACTED].
- d. Apria (a durable medical equipment (DME) service company) [REDACTED] received [REDACTED] on [REDACTED].

2. Failure to maintain accurate device shipment records. [21 CFR 812.140(b)(2)]

Pursuant to 21 CFR 812.140(b)(2), a sponsor shall maintain accurate, complete and current records relating to shipment and disposition of the device. Examples of this failure include but are not limited to the following:

- a. Records of shipment of the investigational device that should include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark reports are not complete.
- b. You failed to document accountability for all devices and components prior to 10/1999 and failed to document accountability for "loaner devices" as well as those shipped back to consignees following repairs.

3. Failure to document all anticipated and unanticipated adverse events. [21 CFR 812.140(b)(5)]

Pursuant to 21 CFR 812.140(b)(5), sponsors are required to maintain accurate, complete and current records relating to an investigation including records of

adverse device effects (whether anticipated or unanticipated) and complaints. Examples of this failure include but are not limited to the following:

- a. You failed to document all adverse events related to device failure, including premature failure of the [REDACTED] and [REDACTED].
- b. You only maintained documentation of adverse events related to re-operations. There is no documentation of whether these adverse events were anticipated or not anticipated.

4. Failure to evaluate and report unanticipated adverse device effects to FDA and the reviewing IRB. [21 CFR 812.46(b)(1) & 812.150(b)(1)]

Pursuant to 21 CFR 812.46(b)(1), a sponsor must immediately conduct an evaluation of any unanticipated adverse device effect, as defined in 21 CFR 812.3(s). After conducting such an evaluation, the sponsor must report the results of the evaluation to the FDA and to all reviewing institutional review boards (IRBs) and to participating investigators within 10 working days after the sponsor receives notice of the effect. 21 CFR 812.150(b)(1). Examples of this failure include but are not limited to the following unanticipated adverse device effects:

- a. [REDACTED] patients died during the course of the [REDACTED]. There is no documentation identifying the cause of death or the date of death, or confirming that you conducted an evaluation of these events. There is also no documentation that reports of any evaluation of these deaths were submitted to FDA or the IRBs.
- b. [REDACTED] dysfunction after less than the expected service life resulted in the replacement of the study device in [REDACTED] subjects. There is no documentation that you evaluated these incidents, and no reports of evaluations were submitted to the FDA or IRBs within 10 working days.
- c. One subject's [REDACTED] failed due to static electricity discharge and was repaired in September 2003. There is no documentation that you conducted an evaluation of this failure, and no report of the evaluation was reported to the FDA or the IRB within 10 working days.
- d. You stated during the inspection that you had assumed that multiple study device failures were due to normal wear on the devices, even when the failures occurred before the end of the expected service life of the devices or their components. When these failures occurred, you did not conduct an evaluation of these events.

5. Failure to ensure proper monitoring of the investigational study and ensure IRB review and approval. [21 CFR 812.40]

Pursuant to 21 CFR 812.40, general responsibilities of sponsors include selecting qualified investigators, providing them with the information they need to conduct the investigation properly, ensuring proper monitoring of an investigation, and ensuring that IRB review and approval are obtained. Examples of this failure include but are not limited to the following:

- a. You failed to monitor the investigational sites to assure that investigators
- b. adhered to the study protocol and to FDA regulations.
- c. You did not have a current copy of the protocol for the device study.
- d. You did not possess adequate documentation demonstrating IRB review and approval of the investigational study.

6. Failure to possess written monitoring procedures. [21 CFR 812.25(e)]

Pursuant to 21 CFR 812.25, an investigational plan shall include written procedures for monitoring the investigation and the name and address of any monitor. There are no written procedures for monitoring your investigational device study.

7. Failure to label the device as investigational. [21 CFR 812.5(a)]

Pursuant to 21 CFR 812.5(a), an investigational device or its immediate package shall bear a label containing the following statement: "CAUTION—Investigational device. Limited by Federal (or United States) law to investigational use." Neither your investigational devices nor their immediate containers bear this required language.

The deviations presented in this letter are not intended to be an all-inclusive list of objectionable practices that may exist. In the course of the FDA investigation, it was discovered that you as a sponsor of an investigational device study did not understand the meaning of "monitoring," did not understand what CRF (case report form) meant, and had no knowledge of the relevant FDA regulations. It is your responsibility as a sponsor of an investigational device study to ensure adherence to each applicable requirement of the Act and all pertinent FDA regulations when sponsoring clinical research.

Within 15 working days of receipt of this letter, please provide a written response, including supporting documentation and specific steps you have taken or will take to correct these violations and prevent the recurrence of similar violations in current and future studies.

Failure to respond to this letter and take appropriate corrective action could result in regulatory action without further notice. Please respond in writing to:

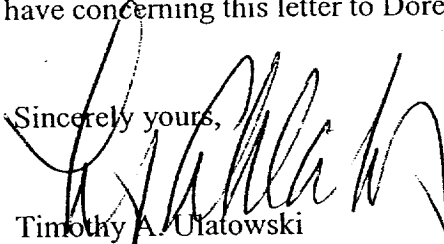
Food and Drug Administration
Centers for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
Special Investigations Branch (HFZ-311)
2094 Gaither Road, Rockville, Maryland 20850
Attn: Doreen M. Kezer, MSN
Branch Chief, Special Investigations Branch

A copy of this letter has been sent to FDA's Florida District Office, Food and Drug Administration, 555 Winderley Place, Suite 200, Maitland, FL 32751. We request that you copy the district on your response.

For further information concerning FDA regulations related to investigational device exemptions please visit our Internet site at <http://www.fda.gov/cdrh/devadvice/ide/index.shtml>. More specific information can be found concerning sponsor responsibilities at the following Internet site: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812&showFR=1&subpartNode=21:8.0.1.1.9.3> Valuable links to related information are included at these sites.

Please direct any questions you may have concerning this letter to Doreen Kezer at (240) 276-0125.

Sincerely yours,



Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health

CC:

