

HF-35



JUN 8 2000

Food and Drug Administration
2098 Gaither Road
Rockville, Maryland 20850

WARNING LETTER

VIA FEDERAL EXPRESS

Mr. Paul Roderique
General Manager
Medical Industrial Equipment Ltd.
Liverton Business Park
Salteron Road, Exmouth
Devon EX8 2NR, U.K.

Dear Mr. Roderique:

We are writing to you because on March 20 through 23, 2000, an investigator from the Food and Drug Administration (FDA) collected information that revealed serious regulatory problems involving your anesthesia machines.

Under a United States Federal law, the Federal Food, Drug, and Cosmetic Act (the Act), these products are considered medical devices because they are used to diagnose or treat a medical condition or to affect the structure or function of the body (Section 201(h) of the Act).

The above-stated inspection revealed that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation of these devices are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. In legal terms, the products are adulterated within the meaning of section 501(h) of the Act, as follows:

- 1. Failure to establish and maintain procedures for implementing corrective and preventive action as required by 21 CFR 820.100(a)(1).** For example:
 - a. Procedures are not established and maintained for analyzing all sources of quality data, including processes, concessions, quality records, and rework, to identify existing and potential causes of nonconforming product and other problems.
 - b. Procedures are not established and maintained employing appropriate statistical methodology to identify existing and potential causes of nonconforming product or other quality problems.

In your response of April 3, 2000, your firm stated that by April 28, 2000, they would write a procedure that describes how they will capture data from such sources as goods in inspection, production inspection, final inspection, suppliers, field service, calibration, concessions, and processes. Problems found at internal audits could be added to this data.

You stated the procedure will describe in detail how your firm will define, document and implement a system for identifying corrective and preventive actions. It will describe how this information will be analyzed using appropriate statistical methods, and how any unfavorable trends will be identified. You say it will also describe how investigations will be conducted, and the effectiveness of documents and any actions taken will be assessed.

Your firm stated that, by the end of May, the system will be in place and being operated. It will be reviewed by a management review of the Quality System which is to take place in May.

This response is not adequate since your firm has not submitted the new procedures.

2. Failure to establish and maintain procedures for investigating the causes of nonconformities relating to product, processes, and the quality system as required by 21 CFR 820.100(a)(2). For example: Procedures are not established and maintained for investigating the causes of nonconformities relating to product, processes, and the quality system.

Your response is indicated in 1 above. This response is not adequate since your firm has not submitted the new procedures.

3. Failure to establish and maintain procedures to document the design input requirements as required by 21 CFR 820.30(c). For example: The approval of design input requirements, including the date and signature of the individual approving the requirements, is not required.

In your firm's response of April 3, 2000, your firm acknowledged the project has been mishandled, and in some aspects you have not followed the design procedures that are in place in the company. They state they will examine the documentation before May 31st and wherever possible will correct it. They state that by May 31st, they will have completed a program to re-train all the engineering staff in departmental procedures that relate to the management and documentation of design projects.

This response is not adequate since the firm has not submitted new procedures or documented the training of their personnel.

- 4. Failure to document, review, and approve the design output before release, as required by 21 CFR 820.30 (d).** For example: The DMR (the design history file for this firm) for the Kite anesthesia machine was not identified, reviewed and approved before transferring the device to production.

Your firm's response is indicated in 3 above. This response is not adequate because your firm has not submitted new procedures or documented the training of their personnel.

- 5. Failure to document the results of design review, including identification of the design, the date, and the individual(s) performing the review in the design history file, as required by 21 CFR 820.30(e).** For example:

- a. Procedures for planning and conducting reviews of the design results at appropriate stages of the device's design development were not followed.

Your firm's response is indicated in 3 above. This response is not adequate because your firm has not submitted new procedures or documented the training of their personnel.

- b. Design reviews were not performed at appropriate times, following the review scheduled in the design plan.

Your firm's response is indicated in 3 above. This response is not adequate because your firm has not submitted new procedures or documented the training of their personnel.

- 6. Failure to designate an individual to review for adequacy and approve prior to issuance all documents established to meet the requirements of Part 820 as required by 21 CFR 820.40(a).** For example:

- a. There is no requirement for documenting the signature of the individual approving the document.

In your firm's letter of April 6, 2000, they state that by April 28th they will have a system for attaching electronic signatures to all relevant electronic documents. The software for this system will have been validated by that date.

They state that because they have more than three hundred documents in their quality system it will take them some time to complete the process of having signatures and records of changes on all their documents. They state that by June 30th they will have changed all the documents that cover the quality, design, production planning, purchasing, and stores functions and that by July 31st all documents will have been reviewed, and all relevant documents will have an electronic signature and records of changes.

This response is not adequate because your firm has not submitted documentation of the changes or copies of the procedures.

- b. Electronic documents are not electronically signed and there is no signed hard copy record.

Your firm's response is indicated in 6a above. This response is not adequate because your firm has not submitted documentation of the changes or copies of the procedures.

- c. The electronic record system lacks computer generated time stamped audit trails.

Your firm's response is indicated in 6a above. This response is not adequate because your firm has not submitted documentation of the changes or copies of the procedures.

7. **Failure to control records as required by 21 CFR 820.40(b).** For example: Change records do not include a clear description of the change, reason for the change, a full description of the change, the identification of the affected documents and the signature of the individual approving the changes. Change records consist of a hidden text (footnote) on the electronic record identifying the change. The date of the change is the date the revised procedure was released and saved in the approved procedure file.

Your firm's response is indicated in 6a above. This response is not adequate because your firm has not submitted documentation of the changes or copies of the procedures.

8. **Failure to establish and maintain procedures for rework, to include retesting and reevaluation of the nonconforming product after rework to ensure the product meets its current approved specifications, and to document rework and reevaluation activities, including a determination of any adverse effect from the rework upon the product, in the DHR, as required by 21 CFR 820.90(b)(2).** For example:

- a. Procedures for rework of nonconforming product are not defined.

In your firm's response of April 3, 2000, they state that the procedures for non-conforming material will be rewritten to describe fully how rework and re-evaluation are documented and defined. They state this rewrite will contain the requirement for the inclusion of all inspection reports and reject forms pertinent to the device in the device history file. The relevant staff members will be re-trained to improve their understanding of the requirement and to teach them how to perform the procedure. They state this will be completed by May 31. They state the nonconforming product and material date and the rejection data will be reviewed as part of the corrective and preventive action requirement.

This response is not adequate since your firm has not submitted the required procedures or documented the training of personnel.

- b. failure to document rework and reevaluation activities, including a determination of any adverse effect from the rework, upon production, in the DHR.

Your firm's response is indicated in 8a above. This response is not adequate since your firm has not submitted the required procedures.

9. **Failure of the device master record to include, or refer to the location of, production process specifications as required by 21 CFR 820.181(b).** For example: There is no device master record including or referring to the location of all device production specifications.

In your firm's response dated April 3, 2000, they state that they accept that their current document that they call a DMR does not fully meet the requirement for a device master record as described in 820.181. They state they will rewrite the procedure for the device master record so that the documents they keep under that name meet the requirements of the FDA regulation. They state any documents they now have which they call a device master record or DMR they will rename and hold as a technical file or device history file, whichever is most appropriate. They state this work will be complete by June 30th, for all the current products made and distributed by MIE.

This response is not adequate since your firm has not submitted their new procedures for the device master record.

10. **Failure to validate computer software used as part of the quality system for its intended use according to an established protocol as required by 21 CFR 820.70(i).** For example: Software such as Excel, Access, and Word used to create and maintain data bases (rejects, complaints, and concessions) and electronic documents, is not validated.

In their response dated April 3, 2000, your firm stated that by May 31st, they will have identified what software is used for data processing, and identified a method or methods for validation and/or verification of the software. Furthermore, they state, they will complete a full and thorough validation of all software that is used for the handling of information or data used in the quality system. This response is not adequate since your firm has not submitted the required validation information.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the closeout of the inspection may be symptomatic of serious underlying problems in your firm's

manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We acknowledge that you submitted to this office an April 3, 2000, response concerning our investigator's observations noted on the form FDA 483. We have reviewed your response and concluded that it is inadequate. An evaluation of specific responses is entered after each one of the deviations listed above.

Given the serious nature of these violations of the Act, the anesthesia machines manufactured by Medical Industrial Equipment may be detained without physical examination upon entry into the United States (U.S.) until these violations are corrected.

In order to remove the devices from this detention, it will be necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that the response is adequate, it will be your responsibility to schedule an inspection of your facility. As soon as the inspection has taken place, the implementation of your corrections have been verified, and you are notified that your corrections are adequate, your devices may resume entry into this country.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Also, no requests for Certificates for Products for Export will be approved until the violations related to the subject devices have been corrected.

Please notify this office in writing, within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations. Include an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to:

James W. Eisele
Consumer Safety Officer
Office of Compliance
Division of Enforcement III (HFZ-343)
Center for Devices and Radiological Health
2094 Gaither Rd.
Rockville, MD 20850

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If you have any questions about the contents of this letter, please contact Mr. Eisele at the above address or at (301) 594-4659, or fax (301) 594-4672. You may obtain general information about all of FDA's requirements for manufacturers of medical devices by contacting our Division of Small Manufacturers Assistance at (301) 443-6597, or through the Internet at <http://www.fda.gov>.

Sincerely yours,

A handwritten signature in black ink that reads "Lillian J. Gill for". The signature is written in a cursive, flowing style.

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