



Food and Drug Administration
2098 Gaither Road
Rockville, Maryland 20850

VIA FEDERAL EXPRESS
WARNING LETTER

Mr. Kevin D'Silva, Managing Director
Ferraris Medical Ltd.
Ferraris House, 2 Aden Road
Enfield, Middlesex, London EN3 7SE
UK

FEB 9 2001

Dear Mr. D'Silva:

We are writing to you because on October 30 through November 2, 2000, an investigator from the Food and Drug Administration (FDA) collected information that revealed serious regulatory problems involving your class II respirometers and peak flow meters. 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 Quality System 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 the identification, documentation, validation, review, and approval of design changes before their implementation, as required by 21 CFR 820.30(i).** For example:

- A. Design control procedures were not followed during the process of adding an alternative method for sterilization, [REDACTED] for the [REDACTED] Respirometers and Peak Flow Meters.

Your written response dated November 6, 2000 stated that the change was viewed as minor to an existing product and that it was covered by the Engineering Change Procedures. Your response also stated that the product is currently undergoing field trials and has not been placed on the market.

Your firm should have followed design control procedures during the process of evaluating an alternative method for sterilization. This process is viewed as an indication change. This response appears to be inadequate.

- B. The lubricant used in the manufacturing of the [REDACTED] Respirometers was changed from traditional natural oil to the [REDACTED] without an engineering change order, F17, and without following design change control procedures.

Your firm's written response dated November 6, 2000 provided documentation of the ECN F17, #1735, showing a change to [REDACTED]. The document is dated July 13, 1998. Apparently, the document was not provided to the investigator at the time of the inspection.

This response appears to be inadequate because there was no evidence provided that showed that all of the design change control provisions to include design validation and design verification, review, and approval prior to implementation were performed and documented.

2. **Failure to establish design input, as required by 21 CFR 820.30(c).** For example, there was no formal documentation for the design input or risk analysis as described in the Design Input section of QAP 400 in regards to adding an alternative sterilization method to the labeling of the [REDACTED] Respirometers and Peak Flow Meters.

Your written response dated November 6, 2000 stated that the firm viewed the proposed change in alternative sterilization as a minor modification to an existing product and that it was covered under the EC procedures only. Your firm failed to follow their own procedures. This response appears to be inadequate.

3. **Failure to establish design output, as required by 21 CFR 820.30(d).** For example, there was no formal documentation as per the Design Output section in QAP 400 in regards to adding an alternative method of sterilization to the [REDACTED] Respirometers and Peak Flow Meters.

Your written response dated November 6, 2000 stated that the firm viewed the proposed change in alternative sterilization method as a minor modification to an existing product and that it was covered under the EC procedures only. Your firm did not follow their operating procedures in the Design and Development Department Operating Procedures. This response appears to be inadequate.

4. **Failure to establish and maintain procedures for validating the device design before implementation, as required by 21 CFR 820.30(g).** For example, there was no design validation before implementation of the design change for the replacement of the natural lubricant to [REDACTED] for the alternative sterilization method planned. The firm stated in QAP 400, Operating Procedure, that all new designs would be submitted to medical organizations for independent design validation. It further stated that in the event of an adverse report at one of the medical organizations, then a Management meeting would be held at Ferraris to review the report and plan the implementation for validation and approval.

Your written response dated November 6, 2000 stated that your firm viewed the proposed sterilization method change as a minor modification to an existing product and was covered by the EC procedures only.

Validation of device design changes should be conducted at your facility before it is sent to medical organizations. Validation should include data to substantiate that the product can meet specifications and will function appropriately for its intended use.

Please review the above regulation and conduct appropriate validation. This response appears to be inadequate.

- 5. Failure to maintain procedures for design review to ensure that formal documented reviews of the design results are planned and conducted at appropriate stages of the design development, as required by 21 CFR 820.30(e).** For example, there were no documented design review meetings provided.

Your written response dated November 6, 2000 included documented review meetings for the [REDACTED] method that apparently was not provided to the investigator at the time of the inspection. This response appears to be adequate but will be verified during the next scheduled inspection.

- 6. Failure to verify and document the device design, as required by 21 CFR 820.30(f).** For example, there were no documented verification activities to evaluate the effectiveness of the [REDACTED] lubricating oil after [REDACTED] Sterilization. Verification after the [REDACTED] change was only performed for the alternative sterilization method (plasma sterilization).

Your written response dated November 6, 2000 stated that the samples of instruments lubricated with [REDACTED] were subjected to [REDACTED] sterilization and inspected although there was no formal report generated. Your firm also stated that the lubricant had been used for 2 years with no adverse reactions to [REDACTED] evident.

There was no documentation to substantiate that the firm did verification activities. Although it was stated that testing of the [REDACTED] change was conducted, was the new lubricant analyzed for how it may affect the rest of the device within its design verification process? This response appears to be inadequate.

- 7. Failure to investigate the cause of nonconforming product or processes, as required by 21 CFR 820.100(a)(2).** For example, the firm did not thoroughly investigate device failures for complaints 776, 778, and 837 for the [REDACTED] Respirimeters that were returned due to corrosion, leakage, and/or low flow problems.

Your written response dated November 6, 2000 stated that procedure QAP 1400 and Customer Complaint Form, F51, have been revised to require a root cause definition for all complaints.

Previously, Form F4 (exhibit 13, page 6), "Quality Concern and Corrective Action Report" also had an area to define a root cause for the problem but personnel did not fill it in. It appears that your firm needs to do some in-house training for personnel so that they are familiar with CAPA and all requirements rather than to just revise the sheets. At the minimum your firm needs a tracking and monitoring system for unresolved investigations/complaints. This response appears to be inadequate.

- 8. Failure to establish and maintain procedures to control all documents, as required by 21 CFR 820.40.** For example, the [REDACTED] Respirimeter finished product test results are occasionally recorded on an interim document, which is not part of the DHR, and then test

results are transcribed to the formal record. This is the second time this observation was cited by a FDA investigator. The first time was at the May 16, 1996 inspection.

Your written response dated November 6, 2000 stated that the person responsible for the interim documentation has been disciplined and that all other employees are aware of the quality requirements. The response did not include any retraining, reinforcement of the Quality System regulations, nor verification that employees are aware of the requirements in regards to document control. This response appears to be inadequate.

9. **Failure to maintain procedures for acceptance of incoming product, as required by 21 CFR 820.80(b).** For example, the [REDACTED] used inside the devices for spindle rotation was not listed as a component and therefore did not go through incoming inspection.

Your written response dated November 6, 2000 provided documentation that [REDACTED] has been added to the ‘Approved Consumables’ list to comply with incoming inspection requirements. This response appears to be adequate, however, it will be verified during the next inspection.

10. **Failure to provide adequate resources for internal quality audits, as required by 21 CFR 820.20(b)(2).** For example, the Managing Director who had direct responsibility for all operations was one of two persons who conducted internal audits at this small firm.

This was not included in the 483 but the investigator discussed with you that more resources were needed in order to train more personnel to do internal quality audits. The investigator explained that an individual with direct responsibility for an operation should not be auditing. As the person with direct responsibility for all operational activities at the firm, the Managing Director, is not a candidate to audit.

The firm explained to the investigator that they were in the process of training other managers to become auditors. This response appears to be adequate but will be verified during the next inspection.

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 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.

It is necessary for you to provide a written response to the charges in this Warning Letter for our review. After we notify you that all responses appear to be adequate, we will request an establishment inspection.

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. Please include any and all documentation to show that adequate correction has been achieved. In the case of future corrections, an estimated date of

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completion, and documentation showing plans for correction, should be included with your response to this letter. Please address your response to:

Edgardo Santiago, Branch Chief
Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Enforcement III (HFZ-343)
2098 Gaither Rd.
Rockville, MD 20850
USA

If you have any questions about the contents of this letter, please contact Brenda Hayden 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,



Larry D. Spears
Acting Director
Office of Compliance
Center for Devices and
Radiological Health

Cc: Mr. Dave Malys, President
Ferraris Medical Inc.
4 Centre Drive
Orchard Park, NY 14127