



M36127

Food and Drug Administration
Rockville MD 20857**WARNING LETTER**
VIA EXPRESS MAIL

APR 4 2000

Mr. Brian G. East, Managing Director
Exmoor Plastics
Lisieux Way
Taunton, TA1 2LB
ENGLAND

Dear Mr. East:

We are writing to you because on January 31 through February 3, 2000, an investigator from the U.S. Food and Drug Administration (FDA) inspected your facility and determined that Exmoor manufactures sterile, implantable medical devices, such as tympanostomy tubes and partial ossicular replacement prostheses.

Under a United States Federal law, the Federal Food, Drug, and Cosmetic Act (Act), these products are considered to be medical devices because they are used to diagnose or treat a medical condition or to affect the structure or function of the body. The above-stated inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act, in that the methods used in, or the facilities or controls used for the manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) requirements set forth in the Quality System (QS) regulation found in Title 21, Part 820 of the U. S. Code of Federal Regulations. The following deviations were identified:

21 CFR 820.20(a)

Failure of management with executive responsibility to ensure that the quality policy has been implemented, understood, and followed at all levels of the organization, as required by 21 CFR 820.20. For example, four out of five employees interviewed were unfamiliar with the quality policy and/or did not know where the quality policy was located. Furthermore, the quality policy specified certain standards (BS NE ISO 9001: 1994; BS EN 46001: 1994; Council Directive 93/42/EEC) that Exmoor Plastics set forth as goals for assuring high quality of design, product and level of service to their customers. The Quality System (QS) regulation was not mentioned.

Your response commits to retraining your workforce, establishing a training document and procedure and documenting such training. This would appear to address this deficiency. However, in order to make such a determination it will be necessary for us to have a copy of your newly established procedures/documentation.

21 CFR 820.22

Failure to have adequate procedures for conducting quality audits, as required by 21 CFR 820.22. For example, Appendix A in Exmoor's quality manual specified that quality audits would be carried out _____ and specified all twenty elements of the ISO standard. This does not encompass all areas that are subject to audit under the QS regulation.

Exmoor's response states that your Quality Management Representative will be receiving audit training and that she will establish and implement a procedure for full internal auditing, which will cover all areas of the QS regulation. In order for FDA to determine the adequacy of your audit procedure, it is necessary that we be provided a copy of your audit procedure.

21 CFR 820.30(c)

Failure to have procedures with a mechanism for addressing incomplete, ambiguous, or conflicting design requirements, and to have input requirements reviewed and approved by a designated individual, as required by 21 CFR 820.30(c). For example, neither Exmoor's quality manual or "Procedure for the Design and Development of Products" documents the methods to be used for addressing incomplete, ambiguous or conflicting design requirements. Furthermore, even though the firm's procedures stated that design input would be reviewed/approved, the signature page for the suction clearance kit failed to provide objective evidence of same since it was not signed.

Your response indicates that Exmoor proposes changes to its Quality Manual and several DMR documents for establishing a mechanism to address incomplete, ambiguous, or conflicting design input requirements. With regard to review and approval of input requirements by a designated individual, Exmoor advises that the lack of signature on the suction kit documentation was due to the fact that the designated individual was out of the country at the time. The kit design input requirements were to be reviewed by the Managing Director. It is indicated that a designee will be responsible if the Managing Director is absent in the future. Again, it will be necessary for us to have copies of the completed procedures in order to determine whether they are adequate to meet the requirements of the QS regulation.

21 CFR 820.30(i)

Failure to establish and maintain design change procedures, as required by 21 CFR 820.30(i). For example, Exmoor could not provide objective evidence that a dimensional change to their Mills Incus Sleeve device had ever been verified to confirm that the pre-firing dimension would, in fact, result in the desired post-firing dimension, taking into consideration that HA shrinks when heated. Also, it was determined that Exmoor does not have documented procedures for the control of pre-production design changes.

Exmoor's response indicates that you have revised your design change proposal to include a procedure to verify that design output meets design input. Your letter acknowledges the failure to verify the dimensional change and states that you have "raised" your internal nonconformance. It is not clear what is meant by this statement. We understand that a procedure for controlling pre-production design changes would be established by April 30, 2000, at which time we would appreciate receiving a copy for review.

Should you have questions as to whether an additional 510(k) is required for this change, your inquiry should be directed to the Division of Ophthalmic and ENT Devices, Office of Device Evaluation, 9200 Corporate Boulevard, Rockville, Maryland 20850. You may also wish to access a copy of our guidance document entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device." It can be found on FDA's website, www.fda.gov, by clicking on the Center for Devices and Radiological Health, then Topic Index, then "P" and scrolling down to Premarket Notification (510(k)). It is the eleventh document listed.

21 CFR 820.30(g)

Failure to have adequate design validation procedures, as required by 21 CFR 820.30(g). For example, Exmoor's quality manual refers to levels of acceptability in their section 4.4.8 "Design Validation." The procedure fails to document how "levels of acceptability" are determined or how the risks are calculated. Furthermore, Exmoor's design validation procedure does not specify that design validation be performed on initial production units, lots, or their equivalents, also required by 820.30(g). This, too, is discussed on page 9.

Your response indicates that Exmoor will be revising their procedures for risk analysis and to ensure that design validation is only performed on initial production units, lots or their equivalents. Copies of these procedures need to be provided to FDA for review.

21 CFR 820.100

Failure to have adequate corrective and preventive action procedures, as required by 21 CFR 820.100. For example, Exmoor received nonconforming grommets (ear tubes) from its vendor. A meeting was held with the vendor and it was determined that the loss of an employee was the cause of the nonconforming device. Exmoor failed to document: the meeting with the vendor, the corrective action taken by the vendor, or that the corrective action promised by the vendor was verified. Exmoor also failed to apply the corrective action to other devices in order to prevent the same problem from arising with those devices.

Exmoor's response indicates that the firm has undertaken training of key staff to ensure that in-house procedures for implementing corrective and preventive actions are followed and closed out as appropriate. Furthermore, it states that _____ meetings have been instituted where corrective and preventive actions will be individually assessed and verified, and that the corrective action procedures have been revised to ensure that changes are applied globally when required.

21 CFR 820.75(c)

Failure to have documented procedures for evaluating when revalidation is warranted, as required by 21 CFR 820.75(c).

Exmoor indicated that the firm utilizes ISO _____ for the validation and control of the firm's _____ sterilization process. However, our investigator was advised that Exmoor has decided _____ dose audits as recommended by the ISO document because of the _____. In addition, our investigator found that no audit of the vendor had been performed since 1996. When asked what procedures Exmoor has in place for determining when revalidation should be performed, it was reported that you have none except for an agreement with _____ that a _____-year review be completed of all dose mapping reports and revalidation performed, as appropriate. Part 820.75 of the QS regulation requires that validated processes be monitored and controlled so that when changes or process deviations occur, a manufacturer will know to review and evaluate the process and perform revalidation when appropriate. Exmoor has no procedures for when changes or process deviations are identified for reviewing and evaluating the process and determining when it is appropriate to revalidate. Exmoor's response states that the firm is looking at their validated processes (e.g., _____ products, clean room revalidations, _____ sterilization, etc.) both for in-house activities and subcontracted activities. It appears that for the in-house activities specific intervals are being established for revalidation, but specific procedures relative to the various activities were not provided. For other activities, the response states that Exmoor would document procedures for identifying the need for revalidation, and that the plan is to visit your subcontractors within the next _____ months. Exmoor will be expected to have established procedures for conducting such visits to their subcontractors. I respectfully suggest that you also refer to 820.50 of the regulation which states that manufacturers shall establish and maintain procedures to ensure that all purchased or otherwise received product and services (e.g., sterilization) conform to specified requirements.

21 CFR 820.25(b)

Failure to establish and document procedures for identifying training needs and ensure that all personnel are trained to adequately perform their assigned responsibilities, as required by 21 CFR 820.25(b). For example, Exmoor personnel admitted to not having established auditor training requirements and that the firm's only method of identifying training needs was through the _____ appraisal system. Our investigator was advised that the firm did not have other mechanisms for identifying training needs, such as feedback provided during an internal audit. Furthermore, it was determined in 1995 that training was needed in the area of _____ and by the end of 1996, it still had not been obtained. The most current personnel appraisals available were from 1996.

Exmoor advised in its response that professional auditor training will be provided and that subsequent in-house training will be conducted and documented for key staff with auditing responsibilities. Furthermore, training needs will not only be assessed during appraisal and counseling sessions, but also during Quality Management Review Meetings, external audits, internal audits and corrective actions. We understand that documentation will utilize a _____ and _____ spreadsheets within the Production Department. It will be necessary for FDA to review the applicable procedures, such as the internal audit and corrective action procedures, and an example of the _____ printout for documenting training once they are developed.

21 CFR 803

Failure to have Medical Device Reporting (MDR) procedures, as required by 21 CFR 803. For example, Exmoor personnel admitted to not having written MDR procedures. While your firm does have a system in place for reporting adverse incidents, there was nothing to address FDA's requirements under MDR. Copies of the regulation and MDR guidance documents are also available on our website by selecting "M" under Topic Index and scrolling down to Medical Device Reporting.

Exmoor's response indicated that a written procedure would be developed and incorporated into the firm's Quality Manual.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is Exmoor's responsibility to ensure adherence to each requirement of the Act and its implementing 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 systems. You are responsible for investigating and determining the causes of the violations identified by FDA. When the violations involve systems problems, you must promptly initiate permanent corrective actions.

We acknowledge that Exmoor submitted to this office a response to our investigator's observations noted on the FDA-483. We have reviewed your response and have concluded that it is inadequate in that it is necessary for FDA to receive copies of your new procedures developed to address the identified deficiencies. At the time that you submit your procedures, you should also indicate when each procedure will be implemented and when your facility will be ready for reinspection by FDA to verify corrections.

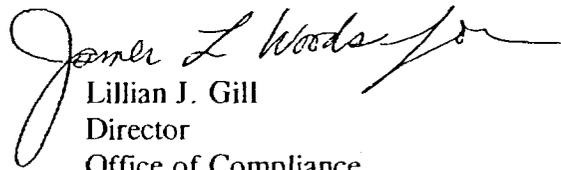
Federal agencies are advised of the issuance of all warning letters about devices so that they may take this information into account when considering the award of contracts. Given the serious nature of the violations that have been identified and the fact that corrections will not be implemented until later this year, all devices manufactured at Exmoor Plastics may be detained upon entry into the United States until these violations are corrected.

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As mentioned above, you need to provide FDA with copies of your new procedures once they have been developed, along with a date that you will be prepared for reinspection. Once our review is completed and an inspection conducted to verify corrections of the identified violations, your products may resume entry into this country.

Your response should be sent to Sharon Kalokerinos, 2094 Gaither Road (HFZ-331), Rockville, Maryland 20850.

Sincerely yours,

A handwritten signature in black ink, appearing to read "Lillian J. Gill". The signature is fluid and cursive, with a long horizontal flourish extending to the right.

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