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## Inspections, Compliance, Enforcement, and Criminal Investigations

### Molteno Ophthalmic Ltd 5/11/10



Department of Health and Human Services

Public Health Service  
Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

MAY 11 2010

#### WARNING LETTER

#### VIA UNITED PARCEL SERVICE

Tess E. S. Molteno  
Managing Director  
Molteno Ophthalmic Limited  
152 Frederick Street  
Dunedin, New Zealand

Dear Ms. Molteno:

During an inspection of your firm located in Dunedin, New Zealand on November 30, 2009 through December 2, 2009, a investigator from the United States Food and Drug Administration (FDA) determined that your firm manufactures the Molteno 3® Glaucoma Drainage Device. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act ("the Act") (21 U.S.C § 321(h)), these products are devices because they are intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or are intended to affect the structure or function of the body.

This inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. We received a response from you dated December 17, 2009, concerning our investigator's observations noted on the Form FDA 483, List of Inspectional Observations that was issued to you. We address this response below, in relation to each of the noted violations. These violations include, but are not limited to, the following:

1. Failure to establish and maintain adequate procedures for implementing corrective and preventative action (CAPA) which include analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, as required by 21 CFR 820.100(a)(1).

For example, your CAPA procedure, PRO/8.5.2/002, does not define how quality data would be analyzed to identify existing and potential causes of nonconforming product as part of determining appropriate actions to correct or prevent recurring quality problems.

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation demonstrating how quality data is analyzed to identify existing and potential causes of nonconforming product.

2. Failure to establish and maintain adequate procedures for implementing corrective and preventive action that

include requirements for investigating the cause of nonconformities relating to product, processes, and the quality system, as required by 21 CFR 820.100(a)(2).

For example, there was no identification and investigation initiated as part of a Corrective Action Request/Non Conforming Product (CAR/NCP) to determine the root cause of the multiple occurrences of inclusions ("black specks") identified on the device plates. In addition, there was no evidence that a Health Hazard Evaluation was performed as part of determining whether any risk to patients exists if the inclusions were to migrate from the device into the patient's eye following implantation.

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation in accordance with your CAPA procedure, PRO/8.5.2/002, demonstrating the identification, initiation, and implementation of a CAR/NCP for the inclusions identified on the device plates. Furthermore, your "Health Hazard Assessment" failed to address the potential risks to patients if the inclusions were to migrate from the device into a patient's eye following implantation.

3. Failure to adequately ensure that where the results of a process cannot be fully verified by subsequent inspection and test, the process shall be validated with a high degree of assurance and approved according to established procedure, as required by 21 CFR 820.75(a).

For example, the manufacturing processes conducted on the injection molding machine (Boy 22S Dipronic) and the package sealer (Zenseal ZS-1100 S/N **(b) (4)**) have not been validated according to established procedures for assuring that the defined operating parameters consistently produce product that meet specifications. In addition, there were no established procedures defining the in-process monitoring requirements necessary to control a validated process.

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation as evidence to show that the validations and equipment qualification activities have been completed for the injection molding machine and package sealer and that the procedures for validated processes have been established, maintained, and implemented.

4. Failure to establish and maintain adequate acceptance procedures, where appropriate, to ensure that specified requirements for in-process product are met. Such procedures shall ensure that in-process product is controlled until the required inspection and tests or other verification activities have been completed, or necessary approval: are received, and are documented, as required by 21 CFR 820.80(c).

For example, there were no requirements for the inspection or verification of the injection molded components (e.g. plates) for assurance that specifications were met prior to being placed into inventory with the necessary documented approvals.

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation as evidence to show that procedures have been or will be established or implemented for acceptance activities of in-process components including the necessary documented approvals.

5. Failure to establish and maintain adequate procedures for validating the device design. Design validation shall be performed under defined operating conditions on initial production units, lots, or batches, or their equivalents. Design validation shall ensure that devices conform to defined user needs and intended uses and shall include testing of production units under actual or simulated use conditions. Design validation shall include [software](#) validation and risk analysis, where appropriate. The results of the design validation, including identification of the design, method(s), the date, and the individual(s) performing the validation, shall be documented in the Device History File, as required by 21 CFR 820.30(g).

For example, the sterilization validation conducted for the Molteno 3 glaucoma drainage implant was incomplete in that it did not include stability testing of the device after moist heat sterilization to determine whether the sterilization process adversely affected the device and potentially render the device as nonconforming and/or adulterated.

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation demonstrating that the devices are not adversely affected by the sterilization process.

6. Failure to establish and maintain procedures for identifying valid statistical techniques required for establishing, controlling, and verifying the acceptability of process capabilities and product characteristics, as required by 21

CFR 820.250(a).

For example, there was no recognized sampling plan methodology incorporating a valid statistical technique to verify the acceptability of the process and take appropriate action when nonconforming components or products are identified that do not meet the acceptable quality limit (AQL).

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation demonstrating that the sampling plan methodology issues have been appropriately addressed.

Our inspection also revealed that your devices are misbranded under section 502(t)(2) of the Act (21 U.S.C. § 352(t)(2)), in that your firm failed or refused to furnish material or information respecting the device that is required by or under section 519 of the Act (21 U.S.C. § 360i), and 21 CFR § 803 - Medical Device Reporting (MDR) regulation. Significant deviations include, but are not limited to, the following:

Failure to develop, maintain, and implement written MDR procedures for internal systems and the documentation and recordation of required information, as required by 21 CFR § 803.17. For example, the firm has not developed, maintained, or implemented written MDR procedures that provide for:

- Timely and effective identification, communication, and evaluation of events that may be subject to MDR requirements;
- A standardized review process or procedure for determining when an event meets the criteria for reporting under this part; and
- Timely transmission of complete medical device reports to manufacturers or to FDA, or to both if required.

We have reviewed your response dated December 17, 2009, and have concluded that it is inadequate because it does not include documentation demonstrating the development, maintenance, and implementation of written MDR procedures.

Given the serious nature of the violation(s) of the Act, the devices manufactured by your firm are subject to refusal of admission under section 801(a) of the Act (21 U.S.C. § 381(a)), in that they appear to be adulterated. As a result, FDA may take steps to refuse these products, known as "detention without physical examination," until these violations are corrected. In order to remove the devices from detention, you should provide a written response to this Warning Letter as described below and correct the violations described in this letter. We will notify you if your response is adequate, and we may need to re-inspect your facility to verify that the appropriate corrections have been made.

Also, U.S. 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. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen (15) working days from the date you receive this letter of the specific steps you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections. 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. Please provide a translation of documentation not in English to facilitate our review.

Your response should be sent to: Ronald L. Swann, Branch Chief, Dental, ENT, and Ophthalmic Devices Branch, WO66-3534, 10903 New Hampshire Avenue, Silver Spring, MD 20993. If you have any questions about the content of this letter please contact: Mr. Swann at (Office) 301-796-5770 or (Facsimile) 301-847-8137.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in the Inspectional Observations, Form FDA 483 (FDA 483), issued at the closeout of this inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to corrected violations and to bring your products into compliance.

Sincerely yours,

/S/

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

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