



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration  
Cincinnati District Office  
Central Region  
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Cincinnati, OH 45237-30977  
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June 26, 2000

**CERTIFIED MAIL  
RETURN RECEIPT REQUESTED**

**WARNING LETTER**  
CIN-WL-00-2448

John B. Armstrong, President  
Chester Labs, Inc.  
1900 Section Road, Suite A  
Cincinnati, Ohio 45237

Dear Mr. Armstrong:

We are writing to you because during an inspection of your firm located at the above address by the Food and Drug Administration (FDA) on March 14-28, 2000, our Investigators collected information that revealed serious regulatory problems involving Electroconductive media (gels and lotions) and Sodium Phosphates Enemas that are manufactured and distributed by your firm.

Under the Federal Food, Drug and Cosmetic Act (the Act), Electroconductive media such as your electrode conductivity gels and lotions are considered to be medical devices. The law requires that manufacturers of medical devices conform with the requirements of the Quality System Regulation (QS Regulation) as specified in Title 21, Code of Federal Regulations (CFR), Part 820.

The FDA inspection revealed that your 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 manufacture, processing, packing, storage or distribution are not in conformance with the requirements of the Quality System Regulation as follows:

Failure to conduct planned formal, documented design reviews of design results at appropriate stages of the device's design development, as required by 21 CFR § 820.30(e). For example, the new electrode gel formulation change (in which inputs were identified on [REDACTED]), did not have formal design reviews identified, conducted or documented.

Failure of the product design inputs to specify acceptance criteria for irritation, sensitivity, preservation challenge or stability, as required by 21 CFR § 820.30(c). For example, the design inputs were specified for the new electrode gel formulation on [REDACTED]. However, the acceptance criteria for the above items were not identified until the design verification/validation and transfer stages, which all occurred on [REDACTED].

Failure of the design verification to confirm that design outputs meet the design input requirements, as required by 21 CFR § 820.30(f). For example, verification of the preservative challenge data for the new electrode gel formula output was not conducted, as no input for these attributes was identified during the input stage of the design project.

Failure to conduct design validation as required by 21 CFR § 820.30(g). For example, your firm failed to conduct design validation activities for skin irritation and sensitivity to support the new electrode gel formulation change that included an increase of [REDACTED] phosphoric acid.

Failure to establish and implement a corrective and preventive actions procedure with adequate controls for preventing the distribution of nonconforming product. For example, for three of thirty-five device history records reviewed by the FDA Investigators, it was observed that during the manufacturing of ultrasound gel and electrode conductivity gel devices, a non-conformance report was completed. While the finished goods were still in the non-conformance status, the Quality Department released the products for commercial distribution. There is no way to determine which portions of the lots were commercially distributed and which portions were considered to be non-conforming product.

Four of the thirty-five device history records reviewed revealed that failure investigations are sometimes not complete and that the investigations are not always documented. For example, no investigation was conducted to determine the cause of low fill and product residue on bottles of conductivity gel in a portion of lot number [REDACTED]-A-ECG.

Failure to assure that the production process is adequately controlled and monitored. Quality control release of products for commercial distribution occurs prior to a batch record review by the Quality Department (QD). The purpose of the review by the QD is to assure that the devices have been manufactured in accordance with the Device Master Record.

The FDA inspection of your medical device manufacturing and distribution operations also revealed that your firm recently made significant changes to the Electroconductive media products you manufacture and distribute. FDA reviewed the records for your firm's Premarket Notification 510(k), K944598 for the Graham-Field Electroconductive media. The FDA notified you via letters dated January 27, 2000 and March 8, 2000 that your firm will need to submit a Special 510(k) and receive FDA clearance prior to marketing your devices with changes you have made.

Under Section 510(k) of the Act, you are required to notify the Food and Drug Administration (FDA) at least ninety (90) days prior to introduction of a device into commercial distribution in the United States. This requirement is accomplished by the submission of a Premarket Notification requirement (510(k)). The information necessary to comply with the premarket notification (510(k)) requirement is found in CFR Part 807, Subpart E - Premarket Notification Procedures.

Our records do not show that your firm obtained marketing clearance before you began offering your new Electroconductive media devices for sale.

The FDA Investigators documented that on [REDACTED] your firm shipped [REDACTED] cases of 8 oz. bottles of Statsign Electrode Conductive Gel to [REDACTED].

Because you do not have marketing clearance from the FDA, to market your modified Graham-Field Electroconductive media, it is in violation of the law. In legal terms, the marketing of the modified Graham-Field Electroconductive media (Gels) causes it to be adulterated under Section 501(f)(1)(B) and misbranded under Section 502(o) of the Federal Food Drug and Cosmetic Act (the Act). The Graham-Field Electroconductive media is adulterated under the Act because you did not obtain premarket approval prior to the marketing of this device, after making significant changes to its formulation that shows that it is safe and effective. The device is misbranded under the Act because you did not submit information respecting the modification of the Graham-Field Electroconductive Gel to the Food and Drug Administration that shows your device is substantially equivalent to other devices that are legally marketed.

Sodium Phosphates Enema manufactured and distributed by your firm is a drug product. During the FDA inspection of your drug manufacturing operation, the FDA Investigators documented deviations from the Good Manufacturing Practice Regulations (Title 21 Code of Federal Regulations, Parts 210 and 211). These deviations cause your drug product to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

Our investigation revealed the following:

Failure to validate the performance of manufacturing processes that may be responsible for causing variability in the characteristics of in-process material and the drug product. For example, validation of the Statistical Process Control program used to monitor the Sodium Phosphates Enema manufacturing process has not been completed. The program has been in use since [REDACTED]

Process validation records for the Sodium Phosphates Enema do not address the problem with container leakage during and after the validation effort. The problem with "leakers" was not investigated.

Failure to establish adequate written procedures designed to assure that the drug products have the identity and strength they purport or are represented to possess. Your firm's Quality System and Standard Operating Procedures contain deficiencies. For example, QSOP 12 allows the release and use of raw materials in production before testing is completed; SOP 100.04 allows the release and shipment of finished product prior to receipt of chemistry or microbiological tests results; and SOP 110.01 allows out-of-specification batches of Phosphates Enema Solution to be adjusted until all specifications are met without requiring an investigation.

Failure to assure that each lot of drug product containers for Sodium Phosphates Enema drug products are not reactive, additive, or absorptive so as to alter the safety, identity, strength, quality, or purity of the drug product beyond the official or established requirements. There is no test data available to assure that containers used for the Sodium Phosphates Enema are not reactive or additive to the drug product.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure 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 FDA 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.

Federal agencies are advised of the issuance of all Warning Letters about drugs and 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.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by The Food and Drug Administration without further notice. Possible actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed.

We received your letter dated May 1, 2000 in response to the Form FDA 483 issued to management at the close of the FDA inspection. Your letter of response was not adequate to correct all of the deficiencies observed at your firm. As outlined above, your firm still needs to take adequate corrective action with regard to your design control system, corrective and preventive actions, and production and process controls for the medical devices you manufacture. In addition, your letter did not address the fact that your firm does not have marketing clearance from the FDA, to market your modified Graham-Field Electroconductive media. For your drug products, corrective action is still needed with regard to process validation, quality control of container/closures, and written procedures for production and process controls. Your letter of response dated May 1, 2000 was made a permanent part of the Establishment Inspection Report File for your firm.

Your response to this Warning Letter should be sent to Evelyn D. Forney, Compliance Officer, Food and Drug Administration, 6751 Steger Road, Cincinnati, Ohio 45237.

Sincerely,

  
Henry L. Fielden  
District Director  
Cincinnati District