



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

CP1

Dallas District
3310 Live Oak Street
Dallas, Texas 75204-6191

January 16, 2001

Ref: 2001-DAL-WL-08

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. Mark W. Aldana
President and Chief Executive Officer
Adven Medical, Inc.
1001 Slaton Highway
Lubbock, Texas 79404

Dear Mr. Aldana:

During an inspection of your firm located in Lubbock, Texas from November 28 to December 8, 2000, our investigator determined that your firm performs reprocessing of medical devices (e.g., diagnostic and ablation catheters, surgical trocars, biopsy forceps, pulse oximeter sensors, and blood pressure cuffs) for hospitals nationwide. These products are medical devices as defined in Section 210(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

The law requires that device manufacturers, including device reproducers, conform to the Quality System (QS) Regulations for medical devices, as specified in Title 21, Code of Federal Regulation (CFR), Part 820.

The inspection documented significant deviations from the Current Manufacturing Practice (CGMP) requirements for devices, therefore, your reprocessed devices are adulterated pursuant to Section 501(h) of the Act.

We have received and reviewed your firm's written response, dated January 8, 2001, responding to our inspectional observations (FDA-483, copy attached) issued, at the completion of the inspection, to Mr. Edmond F. Leser, Quality Assurance Manager. The response indicates that your firm intends to correct all observations within a six-month period and by June 30, 2001. We find your response incomplete because you do not provide a detailed explanation and supporting documentation to address the observations and underlying issues that may have contributed to or resulted in the deficiencies.

Because of the serious nature of the inspectional observations, you are required to take immediate corrective actions to bring your firm's quality systems into compliance with the law. The violations include, but are not limited to, the following:

1. Failure of the management with executive responsibility to ensure that an adequate and effective quality system has been established and maintained [21 CFR 820.20]. For example:
 - a. Established procedures, such as the ETO Sterilization Process, and complaint handling, are not always followed and employee training is not always provided [FDA-483 Items 1 and 16].
 - b. Your firm does not conduct adequate process validations for various cleaning processes, packaging operations, finished device acceptance tests, and ETO sterilization [FDA-483 Items 4, 5, 6, 7, 8, 17, and 18].
2. Failure to review and evaluate process deviations and perform revalidation where appropriate [21 CFR 820.75(c)], and failure to review acceptance activities to ensure that the reprocessed devices meet acceptance criteria prior to product distribution [21 CFR 820.80]. For example, the devices were removed from the sterilization unit after [REDACTED] into the sterilization cycle, and your firm did not review and evaluate the effects of the removal on the sterility of the product. After the product was distributed, the biological indicators were positive for growth. This practice occurred on four occasions [FDA-483 Items 9(b) and 10].

We are also concerned that your firm allows a routine deviation from the ETO sterilization process procedure and there is no review of the growth results of the biological indicators (BI) before distributing the reprocessed devices.

3. Failure to adequately validate the ETO sterilization process, cleaning process, packaging operations, and finished device acceptance tests with a high degree of assurance [21 CFR 820.75]. For example, your firm:
 - a. references the [REDACTED] Standard for Ethylene Oxide Sterilization in Health Care Facilities that excludes the reprocessing of single-use medical devices [FDA-483 Item 4(b)].
 - b. has not established nor monitored the ETO gas concentrations, temperature, and humidity during the exposure phase [FDA-483 Item 4(a)].
 - c. lacks documentation to support why a batch containing [REDACTED] [REDACTED] Devices" is a worst case scenario for a mixed load of different devices in size, density, and composition [FDA-483 Item 4(c)].

- d. has not established preconditioning, exposure and aeration times during the ETO exposure phase [FDA-483 Item 4(d)].
 - e. accepted the results of [REDACTED] as the time for the half cycle with conflicting growth results from the biological indicators. Those indicators showed both growth and lack of growth [FDA-483 Item 4(e)].
 - f. has not conducted tests for sterility, EO residuals, pyrogenicity, and bioburden levels for all types of reprocessed devices [FDA-483 Item 4(g)].
 - g. has not defined acceptance test criteria for the inspection of reprocessed devices during the cleaning process [FDA-483 Item 6(a)].
 - h. lacks documentation to demonstrate that the cleaning process validation is representative of the actual cleaning process used during production (e.g., the number of devices used and the number of cleaning runs are arbitrary) [FDA-483 Item 6(b)].
 - i. lacks documentation to assure that enzymatic and disinfecting solutions can adequately remove foreign materials and reduce the number of particles and microorganisms during the submersion process [FDA-483 Item 4(d)].
 - j. has not verified nor validated the finished device testing to ensure that the devices meet the original manufacturers specifications after reprocessing (e.g., the diagnostic and ablation catheters, trocars, and pulse oximeter sensors) [FDA-483 Item 7].
 - k. has not validated the packaging materials and operations to ensure that the product package maintains the seal integrity and provides a microbial barrier after sterilization [FDA-483 Item 5].
4. Failure to establish and maintain production and process control procedures necessary to ensure that the reprocessed devices conform to their specifications [21 CFR 820.70]. For example, your firm:
- a. has not established nor monitored the ETO gas concentrations, temperature, and humidity during the exposure phase [FDA-483 Item 4(a)].
 - b. has not established preconditioning, exposure and aeration times during the ETO exposure phase [FDA-483 Item 4(d)].
 - c. has not conducted tests for sterility, EO residuals, pyrogenicity, and bioburden levels for all types of reprocessed devices [FDA-483 Item 4(g)].

- d. has not defined acceptance test criteria for the inspection of reprocessed devices (e.g., trocars) during the cleaning process [FDA-483 Item 6(a)].
5. Failure to establish and maintain procedures for verifying or validating changes made to a specification, method, process, or procedure [21 CFR 820.70(b)]. For example:
- a. Your firm is not conducting [REDACTED] tests for sterility, pyrogen, bioburden, and ETO residual for catheters and trocars as required by the Third Party Test Form and Test Failure Procedure (Document #30019, Revision D, Approved 9/30/99) [FDA-483 Item 17].
 - b. In August 2000, your firm purchased, installed, and began using a new sterilization unit, [REDACTED] Model, without qualifying the equipment or validating the sterilization process [FDA-483 Item 8(b)].
 - c. In August 2000, your firm changed its procedures and modified the sterilization process by increasing the sterilization and aeration time from [REDACTED] without justifying the reason for change or re-validating the sterilization process [FDA-483 Item 8(c)].
 - d. In October 2000, your firm changed its procedure and modified the sterilization process by adding the use of [REDACTED], one per [REDACTED], per sterilizer bag to allow for the evaporation of the [REDACTED] [FDA-483 Item 7(d)].
6. Failure to establish and maintain procedures to control the design of the reprocessed devices (e.g., reprocessing of devices labeled for single use) as required by 21 CFR 820.30. For example:
- a. Design input requirements and essential design outputs for the reprocessed devices have not been defined and documented [FDA-483 Items #2(a) and 2(b)].
 - b. Design verification or, where appropriate, design validation (including risk analysis) has not been performed [FDA-483 Items 2(d) to 2(f)]. This violation also includes the lack of adequate process validations for various cleaning processes, packaging operations, finished device acceptance tests, and the ETO sterilization [FDA-483 Items 4, 5, 6, 7, 8, 17, and 18].
 - c. Design history files have not been established [FDA-483 Item 2(g)].

7. Failure to establish and maintain procedures for receiving, reviewing, and evaluating complaints [21 CFR 820.198]. For example:
 - a. Employees are not following the complaint handling procedures in that they are not obtaining and documenting, in detail, the full nature of complaints [FDA-483 Item 14(a)].
 - b. The complaint handling procedures do not address when and how complaint investigations are to be performed [FDA-483 Item 14(b)].

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.

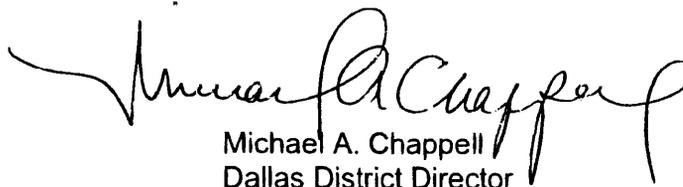
You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

Until these violations are corrected, and FDA has documentation to establish that such corrections have been made, federal agencies will be advised of the issuance of this Warning Letter so that they may take this information into account when considering the award of contracts.

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. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please provide this office in writing within 15 working days of receipt of this letter a report of the specific steps you have taken or will take to identify and correct 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 frame within which the corrections will be completed. Your reply should be directed to Mr. Thao Ta, Compliance Officer, at the above letterhead address.

Sincerely,



Michael A. Chappell
Dallas District Director