



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
91873d

Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3145

October 16, 2001

Ref: 2002-DAL-WL-03

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. Clarence Alfrey, CEO and Treasurer
Ramco Laboratories, Inc.
4100 Greenbriar Drive, Suite 200
Stafford, Texas 77477

Dear Mr. Alfrey:

During an inspection of your firm located in Stafford, Texas, on August 22 through 24, and 28, 2001, our investigator determined that your firm manufactures in-vitro diagnostic (IVD) devices, such as the Cand-Tec Latex Agglutination Test, Human Transferrin Receptor [TfR] Immunossay, various Ferritin Tests, von Willebrand Factor Immunoassay, and Eporia Radioimmunoassay, and repacks pregnancy test kits. These products are medical devices as defined in Section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act).

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 their manufacturing, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System Regulations, as specified in Title 21, Code of Federal Regulation (CFR), Part 820. Significant GMP deviations include, but are not limited to, the following:

1. Failure to establish and maintain procedures for management review [21 CFR 820.20(c)] and failure to document the appointment of a management representative [21 CFR 820.20(b)(3)] [FDA-483 Item 6].

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2. Failure to establish and maintain procedures for quality audits [21 CFR 820.22]. For example, your Quarterly Audit Check List, dated 1/12/01, does not cover audits of management controls, purchasing controls, document controls, non-conforming product, corrective and preventive action, storage, and device master records [FDA-483 Item 1(a)].
3. Failure to document personnel training [21 CFR 820.25]. For example, your firm did not maintain training records of the [REDACTED] auditors performing internal quality audits [FDA-483 Item 1(b)].
4. Failure to establish and maintain procedures for the identification, documentation, evaluation, segregation, and disposition of the non-conforming product [21 CFR 820.90]. For example:
 - (a) There is no documented justification explaining why your firm decided to accept and release TFR assay lot# 94-38 which had out-of-range normal control values [FDA-483 Item 2]; and
 - (b) Our inspection confirmed that your employees had no disposition records for the TFR assay kits, lots 94-36 and 94-37, or conjugate remaining in-house at the time of your 6/7/00 recall of the TFR assay. The recall is due to an excessive level of non-specific binding of the conjugate.
5. Failure to establish and maintain procedures for analyzing processes, work operations, complaints, and other quality data sources to identify existing and potential causes of non-conforming product and to detect recurring quality problems [21 CFR 820.100 (a)(1)]. For example, your firm did not maintain documentation of any systematic or statistical analysis of quality control test data and customer complaints [FDA-483 Item 3(a)].
6. Failure to establish and maintain procedures for the identification, documentation, validation or verification, review, and approval of design changes before their implementation [21 CFR 820.30(i)]. For example, your firm lacks accelerated stability test results and conclusions to confirm that the original product expiration date of [REDACTED] months has not changed after a change in conjugate was initiated on [REDACTED] [FDA-483 3(c)].

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7. Failure to establish and maintain procedures to control changes to documents [21 CFR 820.40]. For example, you did not maintain change records, including a description of the change and the signature of the approving individual(s), for the previous three revisions of the Quality Audit Checklist, dated 6/22/99, 12/10/99, and 1/12/01 [FDA-483 Item 5]. This deviation is also a similar objectionable condition observed during the previous two Texas Department of Health (TDH) inspections of your firm on May 11 through 13, and December 15 through 16, 1999.
8. Failure to maintain complete records of corrections and removals not required to be reported to FDA [21 CFR 806.20(b)]. For example, your records did not document the justification for not reporting your 6/7/00 recall of Tfr assay lots 94-36 and 94-37 to FDA [FDA-483 Item 3(b)].

We have received your firm's response letter, dated September 5, 2001, responding to our list of inspectional observations (FDA-483 - copy enclosed) issued to Mr. Jeffrey B. Grubb, President, at the completion of the inspection. You promised to modify your firm's quality system to address the observations. Your response is incomplete because you have not provided any detailed explanations, supporting documentation, and status reports of corrective actions to show what steps your firm has taken or will take to correct the observations. We also note that the TDH has issued two state warning letters for two recurring GMP violations observed during the inspections on May 11 through 13, and December 15 through 16, 1999. The violations concerned your firm's lack of compliance with document change controls and design controls.

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 close 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.

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You should take prompt action to correct these violations. Failure to promptly correct these violations 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 Thao Ta, Compliance Officer, at the above letterhead address.

Sincerely,



Michael A. Chappell
Dallas District Director

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Enclosure