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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 526-6009

October 30. 1998

WARNING LETTER

Raymond F. Akers, Jr., PhD.
President
Akers Laboratories, Inc.
201 Grove Road
Thorofare. New Jersey 08086

File No.: 99-NWJ-03

Dear Dr. Akers:

During an inspection of your facility located at 201 Grove Road, Thorofare, NJ, between the period of July 21 and August 4, 1998, Investigators from this office determined that you manufacture and distribute for export, HealthTest™ HIV 1 + 2 Rapid Assay Test Kits and Hepatitis B Surface Antigen (HBsAg) Test Kits. These test kits are devices within the meaning of section 201(h) of the Federal Food, Drug and Cosmetic Act (the Act). The devices have been exported in violation of section 802(f)(1) of the Act, since the investigators documented serious violations that cause these devices to be adulterated within the meaning of section 501(h) of the Act.

These devices are considered adulterated under section 501(h) of the Act, in that the methods used in, or the facilities or controls used in the manufacture, processing, packaging. storage or distribution of HealthTest™ HIV 1 + 2 and HBsAg assay test kits. are not in conformance with the Quality System Regulation for Medical Devices, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

I - Quality System Regulations

1. Failure to establish and maintain procedures for the identification, documentation, validation, or where appropriate verification, review and approval of design changes before their implementation as required by 21 CFR 820.30(i). For example:

   - There is no validation data to support labeled performance characteristics for sensitivity and specificity for any rapid assay test kits.
   - There are no established process controls to ensure that specifications are met during production.

2. The Device Master Record for assay test kits is incomplete and contains obsolete information. For example:

   - Concerning the HealthTest™ HIV 1 + 2 Assay Test Kits, the Device Master Record does not specify when performance testing is required during production and lacks testing procedures. Also, the DMR lacks specific process specifications for mixing the bulk reagent.
   - Procedure 0-22 in the DMR requires associated controls to be packaged with the finished kits. However, controls are no longer manufactured or packaged for any test kit.

3. Device History Records for assay test kits contained examples of documentation and calculation errors. For example:

   - The DHR for HIV Latex Reagent, lot 2-022698-03, contained a calculation error resulting in the incorrect amount of Glycine Buffer Volume (GBV) being added.
   - The DHR for HBsAg Ampules, Lot 2-041798-01, does not account for 30 ml of reagent.

4. There are no stability studies for finished kits to support established expiry dates. For example:

   - The expiry date for HealthTest™ HIV 1 + 2 Combo Kit is established one year from the manufacturing date for latex, however, this is not consistently applied. For example, Kit 4-052798-01 was assigned a 19 month expiry date from the manufacturing date of latex used.
   - For Hepatitis B Reagent Ampule Lot 2-041798, the expiration date was changed from October 8, 1998 to April 8, 1999 without explanation.

5. The acceptance activities of raw materials used in production, are lacking in documentation to demonstrate that components and vendors will meet pre-determined specifications. For example:

   - Raw materials (antigens and antibodies) labeled for "Research Use Only" are utilized in the production of test kits.
   - There were no approved specifications of raw materials.
   - There is no documented evaluation for the suppliers of raw materials used in finished kits.
   - The in-process leak test for the acceptance of reagent-filled ampules is not documented.

6. There is no documented Installation Qualification or Operational Qualification for equipment used during production, such the Semi-Automatic Vial Sealer, Pipette Heat Healer and Diagnostic Strip Press.

7. There is no assurance that the cleaning procedures for the filling pump, used to fill the HIV antigens and the HBsAg antibodies, effectively removes chemical microbiological or residual reagents.

8. There are no controls for computer generated labeling used for product inserts. It was noted during the inspection that finished HealthTest™ HIV 1 + 2 and HBsAg test kits were relabeled from "For in vitro use only" to "For Research Use Only".

9. During the inspection, numerous examples of failure to follow established procedures were noted. For example:

    - Failure to follow SOP-005 "Approval of Product Labeling", in that product inserts for the HealthTest™ HIV 1 + 2 Test Kits were changed from a 1:4 to 1:10 serum dilution and products were shipped, prior to the approval date for the dilution change.
    - Failure to follow SOP "Raw & In-process Material Control", in that ABO Covers lot 1-032698-01 in the in-coming quarantine area were labeled as "On-Hold" and "Released", with the same date.

10. There are no approved written procedures regarding the following areas:

    - Design changes, including identification, documentation, validation, verification, review and approval of design changes.
    - Shipment of products labeled "For Export Only", or how kits are packed during shipment.
    - Rework activities.

II - Exporter issues

Your firm has not demonstrated due diligence in that there is no documented evidence that the domestic distributors/exporters are aware that these devices are intended for export use only, nor do they acknowledge that the test kits are unapproved devices.

Additionally, your firm is in violation of section 802(g) of the Act, since you have failed to comply with the requirements outlined in the statute, as follows:

1. A simple notification was not provided to the Secretary identifying the device when the exporter began to export such device to any country listed in section 802(b)(1)(A)(i) or (ii) of the Act. For example, HealthTest™ HIV 1 + 2

Assay test kits were exported to Madrid, Spain on June 16, 1998 and HBsAg assay test kits were exported to London, England on June 2, 1998.

2. A simple notification was not provided to the Secretary identifying the device and the country to which such device was being exported when the exporter first began to export a device to a country not listed in section 802(b)(1)(A)(I) or (ii) of the Act. For example, HealthTest™ HIV 1 + 2 Assay test kits were exported to India on May 22, 1998, without notification.

3. Documentation collected during the inspection concerning export of test kits to Nigeria and Saudi Arabia is an evaluation of the HealthTest kit, not a foreign authorization for the importation of the unapproved device.

4. Documentation collected during the inspection concerning export of test kits to Russia provides no English interpretation of the document.

III - Labeling Issues

In addition, these devices are considered misbranded within the meaning of section 502(b) of the Act in that the address of the manufacturer is not included on the label of the packaged test kits. Examples of labeling (kit, component and product insert) collected by the Investigators during the recent inspection have been reviewed by both the Center for Biologics Research and Evaluation and the Center for Devices and Radiologic Health and the following comments should be noted:

1. Labeling "For Research Use Only" is not sufficient. Labeling should state "For Research Use Only. Not for diagnostic procedures". For example, HealthTest™ HIV 1+2 Whole Blood Assay - kit label.

2. Labeling "For Investigational Use Only" is not accurate. Labeling should state "For Investigational Use Only. The performance characteristics of this product have not been established". For example, HealthTest™ HIV 1+2 Assay - kit label.

3. Labeling should state "For Export Only" and/or "Not for use in the U.S." For example, HealthTest™ HIV 1+2 assay - IVD use only insert, dated April 4, 1998.

4. Labeling requires use of controls supplied with the test kit, when no controls are supplied. For example, HealthTest™ HIV 1+2 assay - IVD use only insert dated April 4, 1998.

5. Labeling contains the firm name only and does not contain the place of business. For example, HealthTest™ HBsAG assay - kit label.

6. Test kits that are labeled for research only should not contain "Performance Characteristics" or "Interpretation of Results". For example, HealthTest™ HBsAg assay.

7. The July 1998 insert for the HealthTest™ HIV 1+2 Assay for Investigational Use Only, should not contain "Performance Characteristics".

8. The HealthTest Serum dilution kit (for *in vitro* use only) label does not have a declaration of the established name and quantity, proportion or concentration of each reactive ingredient. For a reagent derived from a biological material, the source should be stated as well as a measure of its activity. Additionally, no lot or control number or expiration date is listed for this kit.

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 the letter and in the Inspectional Observations (FDA 483), issued to you during 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, and promptly initiating permanent corrective actions.

Federal agencies are advised of the issuance of all Warning Letters about devices so they may take this information into account when considering the award of contracts or issuing certificates of export.

Additionally, no pending applications for Premarket approval (PMAs) will be approved and no premarket notifications [510(k)s] will be found substantially equivalent for products manufactured at the facility in which the above GMP violations were found until the violations 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. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

We are in receipt of your written responses, dated August 10 and 31, 1998, regarding the FDA483 List of Inspectional Observations, issued to you at the conclusion of the inspection. Your responses have been reviewed and in general, found to be inadequate. A more detailed reply to each FDA483 point will be sent to you under separate cover.

Please notify this office in writing within 15 working days of receipt of this letter, of any additional steps you have taken to correct the noted violations, including each step that has or will be taken to correct the current violations and the timeframe within which the corrections will be completed. Corrective actions should also indicate the person responsible for effecting correction, and include any supporting documentation indicating correction has been achieved.

If corrections cannot be completed within 15 working days, state the reason for the delay and the timeframe within which corrections will be completed. Please include in the response your intentions regarding the continued illegal exportation of these kits.

Please direct your reply to the Food & Drug Administration, New Jersey District Office, 10 Waterview Blvd, 3rd Floor, Parsippany, NJ 07054, Attn: Mercedes Mota, Compliance Officer.

Sincerely,

for Douglas Ellsworth
Director
New Jersey District, FDA

CERTIFIED MAIL -
RETURN RECEIPT REQUESTED