U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Iso-Tex Diagnostics, Inc 12/3/10

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Dallas District
4040 North Central Expressway
Dallas, Texas 75204-3128

December 3, 2010

Ref: 2011-DAL-WL-03

WARNING LETTER

CERTIFIED MAIL
RETURNED RECEIPT REQUESTED

Mr. Thomas J. Maloney, President
Iso-Tex Diagnostics, Inc.
1511 County Road 129
Friendswood, Texas 77549

Dear Mr. Maloney:

During our May 4, 2010 to June 2, 2010 inspection of your pharmaceutical manufacturing facility, Iso-Tex Diagnostics, Inc., located at 1511 County Road 129, Friendswood, Texas, investigator(s) from the Food and Drug Administration (FDA) identified significant violations of Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211. These violations cause your drug product(s) to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with CGMP.

Specific violations observed during the inspection include, but are not limited, to the following:

1. Your firm has not thoroughly investigated the failure of a batch or any of its components to meet its specifications whether or not the batch has already been distributed [21 C.F.R. § 211.192]. For example,

   a. Your firm failed to thoroughly investigate positive sterility test results (i.e., **(b)(4)** and **(b)(4)** isolates) for both the **(b)(4)** and **(b)(4)** canisters in the sterile injectable drug product, Glofil I-125 (lot G92006-82). Your investigation concluded that the samples were contaminated by the environment since routine environmental monitoring identified identical bacterial organisms. However, your firm failed to consider that your drug product may also be contaminated.

   b. Your firm failed to thoroughly investigate positive sterility test results in the sterile injectable drug product, Jeanatope I-125 (lot J101702-25B). Your firm claimed that the initial result was a false positive because of a defective filter in the sterility test kit. As a result, your firm re-sampled and conducted sterility testing for **(b)(4)** additional drug product samples and observed a single positive result for a **(b)(4)** species. Your investigation failed to determine the root cause of the positive test result observed during the sterility retest.

2. Your firm has not established appropriate written procedures for validation of all aseptic and sterilization processes designed to prevent microbiological contamination of drug products purporting to be sterile [21 C.F.R. § 211.113(b)]. For example,

   a. Your firm has not validated the **(b)(4)** Filter used in the sterilization of your drug products, including Glofil I-125, Jeanatope I-125, and Megatope I-131.

   b. Your firm has not established procedures for the practice of moving the **(b)(4)** Air Sampler between the **(b)(4)** hood and the surrounding **(b)(4)** areas. This sampler transfer between the two areas was observed during the filling of Megatope I-131 (lot V101105-441).

   c. Your firm's Standard Operating Procedure (SOP) 3004 entitled, "Sanitization of an Environmentally Controlled Area," does not describe the sanitization of the plastic totes used to transport supplies from the uncontrolled areas to the **(b)(4)** environment. In addition, your SOPs do not require the use of sterile or sterile filtered bleach and water for sanitization of your controlled areas.

3. Your firm does not have adequate control systems to prevent contamination of your floors, walls, and ceilings of smooth, hard surfaces that are easily cleanable [21 C.F.R. § 211.42(c)(10)(i)].

   For example, the conditions of your walls and ceilings in the Glofil I-125 and Megatope I-131 production areas are not conducive to cleaning. These walls were observed to be chipped and cracked, and lacking a smooth surface texture to allow proper cleaning.

4. Your firm failed to provide exhaust systems or other adequate systems to control contaminants in areas where air contamination occurs during production [21 C.F.R. § 211.46(c)].

   For example, your firm has failed to maintain pressure differentials between classified rooms to control ingress of contamination. This failure to maintain the pressure differentials was the result of your Heating, Ventilation, and Air Conditioning (HVAC) unit operating in an automatic mode (temperature set point controls fan) when the Megatope I-131 and Glofil I-125 production suites were not in use.

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations. It is your responsibility to assure compliance with all requirements of federal law and FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates, or approval of pending drug applications listing your facility, until the above violations are corrected. FDA may re-inspect to verify corrective actions have been completed.

In addition, we are concerned about your firm's transition to using the **(b)(4)** Filters for drug product sterilization. This modification of your sterile filtration process is considered a major change under 21 C.F.R. § 314.70(b)(3)(vii), especially if the change constitutes a change beyond the previous validated parameters. Please provide a comparison of the previous filtration parameters with the **(b)(4)** Filters parameters, including flow, total filter volume, microbial retention data summaries, and controls used to evaluate the new filter system. Further, please provide a date when

this change occurred to your sterile filtration process.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction. Additionally, your response should state if you no longer manufacture or distribute any of the drug products manufactured at this facility, and provide the date(s) and reason(s) you ceased production.

Your reply should be sent to following address: U.S. Food and Drug Administration, 4040 N. Central Expressway, Suite 300, Dallas, Texas 75204, Attn: Shari J. Shambaugh, Director of Compliance Branch.

If you have any questions regarding this letter, please contact Mr. Thao Ta, Compliance Officer at (214) 253-5217.

Sincerely,

/s/

Reynaldo R. Rodriguez, Jr.
Dallas District Director

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