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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region m2599n

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

Telephone (973) 526-6009

CERTIFIED MAIL -
RETURN RECEIPT REQUESTED

WARNING LETTER

April 26, 1999

Thomas S. Freund, Ph.D., President
Health Science Laboratories and Services, Inc.
One South Corporate Drive
Riverdale, New Jersey 07457

File No: 99-NWJ-21

Dear Dr. Freund:

An inspection of your control testing laboratory located at One South Corporate Drive in Riverdale, New Jersey, was conducted from January 13 through February 1, 1999, by an Investigator from this office and two Microbiologists from the New York District Office, Food & Drug Administration. This inspection revealed significant deviations from the current Good Manufacturing Practice (cGMP) regulations for Medical Devices, found in Title 21, Code of Federal Regulations. Such deviations cause these products to be adulterated with the meaning of Section 501 (a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

The significant cGMP deviations noted are as follows:

1. There was no raw data to support microbiological test results reported to clients, for example:
    a. Porcine aortic heart valves, HSL Lots 9814020A, 9814020B, 9814020C and 9814020E were reported as sterile, yet there was no evidence that sterility tests were conducted.
    b. Corning vials HSL lot 9827110, reported results of no bacterial growth after 14 day media incubation, however the microbiology work sheets indicate the media was not read past the 9th day.

2. **Out of specification test results were not reported, nor investigated, for example:**

   Sterility tests for biological indicators used in Ethylene Oxide sterilization HSL Lots 9822420, 9829405, 9830913, 9832111, 9832420, 9830912 and 9829405 indicated positive micro growth on the analyst's worksheets. However, this information was not reported on the test reports to the clients, nor were the results evaluated and investigated.

3. **There is no documented review of the laboratory worksheets used to record raw data by the Quality Unit to assure this information is accurately reported in the final test records.**

4. **There are no quality control provisions regarding the preparation, handling and testing of media used to perform microbial analysis. For example:**
   a. **Autoclave cycles used to sterilize microbial media were not validated.**
   b. **There are no established procedures or protocols regarding the release of prepared media. The Quality Unit does not review media preparation worksheets to assure that acceptable sterilization cycles and pH ranges have been met.**
   c. **Growth promotion studies are inadequate. Challenge organisms used for these studies were observed to be beyond their expiration date.**
   d. **Multiple containers of dehydrated media, used as raw materials in media preparation, were observed to be out of expiry. An example was found in which Lactose Broth, Lot 9209-138, Expiration 10/96, was used in media prepared to conduct microbial limits testing on January 15, 1999 for [redacted] HSL Lots 9835113 A-E.**
   e. **There is no system in place to assign expiration dates to prepared media.**

5. Deviations from procedures were noted. SOP LAB-0050 prohibits use of remaining media after sterility testing. However, during the inspection Investigators observed remaining media being stored for future testing.

6. There is no documentation to support that alternative test methods used, were validated or shown to be equivalent to USP methodology. For example,
   a. Antibiotic assay for Gentamicin Sulfate Cream and Triple Antibiotic Ointment
   b. Bacteriostasis/Fungistasis (growth promotion)
   c. Antimicrobial effectiveness (preservative effectiveness)
   d. Bacterial endotoxin (LAL)
   e. Microbial limits testing

7. **During sterility testing for corning vials, HSL Lots 9901912, 9901154 and 9901153, disinfecting practices observed in use were not evaluated to determine the effect on prepared media or test articles. For example, the 20% commercial bleach solution sprayed directly on the employee and work surface areas was observed to be dripping onto the test article and media used during the test.**

You will note that some of the above deviations are similar to issues previously cited in Warning Letter 98-NWJ-33, dated August 6, 1998, which concerned the testing of finished pharmaceuticals. The corrective actions implemented at that time were ineffective in preventing the current inspectional findings.

The above is not intended to be an all-inclusive list of deviations of your testing facility. As a contract testing laboratory, you are responsible for assuring that your overall operation is in compliance with all requirements of the Federal Food, Drug and Cosmetic Act and the regulations promulgated under it. You should take prompt action to correct these conditions and establish procedures to prevent their reoccurrence. Failure to promptly correct these deviations may result in further regulatory action without notice, such as injunction.

We have received your written response, dated February 9, 1999, concerning the inspectional observations cited on the FDA483, dated February 1, 1999. While many commitments were made in your response, based on your previous inspectional history, we are unable to assess the adequacy of your response. You will need to demonstrate compliance with cGMPs regarding the testing of finished pharmaceuticals and devices during future inspections. Until FDA has confirmed that these deficiencies have been corrected and your firm is in compliance, we will not recommend approval of new drug applications listing your firm as a testing laboratory.

We note your request for a meeting with FDA management. However, a meeting at this time would not be appropriate until you can provide evidence of corrective actions applied globally to drug and device testing. We recommend that you conduct a thorough evaluation of your operations prior to any future requests for a reinspection or meeting with District officials.

Please notify this office in writing, within 15 working days of receipt of this letter as to the status of the corrective actions outlined in your response. Please direct your response to the Food and Drug Administration, New Jersey District Office, 10 Waterview Blvd., 3rd Floor, Parsippany, New Jersey 07054, Attn: Mercedes Mota.

Sincerely,

Edward H Wilkins, for

Douglas I. Ellsworth
District Director
New Jersey District Office