



DEPARTMENT OF HEALTH & HUMAN SERVICES

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New York District

Food & Drug Administration  
850 Third Avenue  
Brooklyn, NY 11232

**WARNING LETTER**

**CERTIFIED MAIL**  
**RETURN RECEIPT REQUESTED**

Christine Liuzzi, President  
Liuzzi Microbiology Laboratory, Inc.  
212 Maple Street  
Islip, NY 11751

October 29, 1998

Ref: NYK-1999-6

Dear Ms. Liuzzi:

During an inspection of your contract testing laboratory located in Islip, New York conducted on September 10 through 17, 1998, our investigators documented deviations from Current Good Manufacturing Practice (CGMP) for Finished Pharmaceuticals Regulations (Title 21, Code of Federal Regulations, Parts 210 and 211) concerning your procedures for testing drug products for, but not limited to, [REDACTED]. Your laboratory is considered an extension of a pharmaceutical manufacturer's own facility under 21 CFR 200.10. These deviations cause drug products that you test to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). The deviations include, but are not limited to, the following:

1. Failure to have adequate laboratory controls for sampling and testing various drug products and components to determine their conformance to compendial specifications (21 CFR 211.160), such as:

a. Preparatory testing was not performed on all drug product samples being tested for microbial limits as required by the USP test procedures. These include your sample nos. 598093, 698194, 898089, 898090, 898099, 898137, 898138, and 898165.

b. Drug product samples undergoing microbial limits testing were not weighed to ensure delivery of the specified amount of sample into the test media as required by the USP test procedures. The investigators also observed that no attempts were made to disperse samples throughout the test media during microbial limits, total plate count, and yeast/mold testing.

c. Your laboratory's SOPs state that process water samples are to be tested in accordance with the current Standard Methods for the Examination of Water and Wastewater. However, standard plate count agar and lactose broth were being used for

this testing instead of R2A or heterotrophic plate count agar, and laurel sulfate tryptose broth as called for by the current test method.

d. SOPs for growth promotion testing of in-house prepared media did not specify the quantity of organisms to be inoculated.

2. Failure of the laboratory records to include complete data derived from all tests necessary to assure compliance with established specifications and standards (21 CFR 211.194(a)), such as:

a. Microbial test records did not document the actual use and readings of positive controls associated with each drug product sample tested.

b. The autoclave cycles log did not document the start and end times of the actual sterilization cycles employed, nor did it include the identification of the autoclave that was used for each sterilization run.

c. On September 14, the investigators observed a load of bottled media being sterilized in autoclave #2, and the prior load from this autoclave consisting of tubed media being cooled on a counter top. Their review of the autoclave log showed no entry had been made for either of these two loads.

d. On September 16, the investigators observed a load of VJ agar being sterilized in autoclave #2, and the prior load from the same autoclave consisting of buffered water being cooled on a counter top. Neither of the loads had yet been entered in the autoclave log. When log entries were made later that day, they identified the use of a maximum recording thermometer in the loads. The investigators observed no use of this thermometer.

3. Failure to calibrate instruments, apparatus, gauges, and recording devices at suitable intervals in accordance with established written procedures, and to maintain complete records of the calibrations (21 CFR 211.160(b)(4) and 21 CFR 211.194(d)), such as:

a. The outside contract service records showed scheduled 1998 calibrations of the autoclave pressure gauges were not performed as required by the laboratory's SOPs.

b. Recent calibrations of the autoclave liquid-in-glass thermometer gauges showed temperature errors of as much as 2.8 degrees centigrade with no corrective actions taken. The laboratory SOPs do not address any specification for accuracy.

c. Autoclave temperature gauges are calibrated at several readings up to 105 degrees centigrade, but not at the sterilization temperature of 121 degrees centigrade.

d. Thermometer no. 8865, which is used to perform in-house accuracy checks on the rectal thermometers used for rabbit pyrogen testing, has not been calibrated since

1994. Laboratory SOPs require yearly calibration. Further, the records of the in-house accuracy checks do not identify the specific rectal thermometers that were checked.

e. The May 1998 outside contract service records for the calibration of all laboratory thermometers do not report any test results. This is contrary to the May 1997 calibration records, which indicate either that no correction is needed or that temperature differences noted require a specified correction factor.

4. Failure to have adequate laboratory controls for the use and disposition of laboratory media (21 CFR 211.160(a) and 211.194(c)). For example, the investigators observed active stocks of powdered microbial test media bearing expired use dates. These included Levine's EMB, fluid thioglycollate medium, heart infusion broth, selenite cystine broth, and Kligler's iron agar.

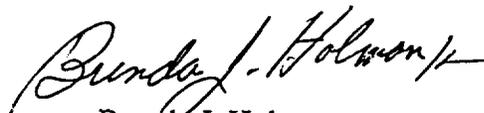
Neither the above identification of CGMP violations nor the inspectional observations (Form FDA 483) (copy enclosed) presented to you at the conclusion of the inspection is intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence with each requirement of the Act and its implementing regulations. Federal agencies are advised of the issuance of all warning letters about drug products so that they may take this information into account when considering the award of contracts. Additionally, pending Antibiotic Form 6, NDA, ANDA, or export approval requests may not be approved until the above violations are corrected.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action without further notice. These actions include, but are not limited to, seizure and injunction.

You should notify this office in writing, within 15 working days after receipt of this letter, of (1) each step that has been or will be taken to completely correct the current violations and to prevent the recurrence of similar violations; (2) the time within which the corrections will be completed; (3) any reason why the corrective action has not been completed within the response time; and (4) any documentation necessary to show the corrections have been achieved.

Your reply should be sent to the attention of Bruce A. Goldwitz, Compliance Officer, Food and Drug Administration, 850 Third Avenue, Brooklyn, NY 11232, Tel. (718) 340-7000 ext. 5507.

Sincerely,



Brenda J. Holman  
District Director