



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region *m3882n*

Telephone (973) 526-6010

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

June 26, 2000

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Dr. Manohar Bhambhani, President
Sciencetech Laboratories, Inc.
197 Meister Avenue
North Branch, New Jersey 08876

FILE NO.: 00-NWJ-42

Dear Dr. Bhambhani:

The U.S. Food and Drug Administration, New Jersey District, conducted an inspection of your testing laboratory located at 197 Meister Avenue, North Branch, NJ, from May 8 through May 24, 2000. The inspection revealed significant deviations from Current Good Manufacturing Practice regulations (Title 21 Code of Federal Regulations (CFR), Parts 210 & 211) regarding the performance of analyses, lack of validation of test methods, documentation practices, and general laboratory practices. These deviations cause articles of drugs, whether analyzed for release for further manufacture or release for commercial distribution, to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug and Cosmetic Act (the Act).

- 1) Regarding the performance of analyses at your facility, numerous random, inexplicable, and unapproved changes were made to analytical methods. For example:
 - a) During Organic Volatile Impurities (OVI) testing conducted for [REDACTED] the appropriate methods specified in the USP were not followed. Samples of Magnesium Stearate, Propoxyhene Napsylate, and Potassium Chloride were analyzed together. However, the USP indicates that each of these three products should be analyzed by a different OVI method. Additionally, Magnesium Stearate and Clorazepate Dipotassium were analyzed together, although the OVI methods specified in the USP are different. The results from these modified methods were reported to [REDACTED] as having been obtained by the USP method.

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- b) [REDACTED] supplied an analytical method to Sciencetech Laboratories for use during testing of their [REDACTED] Ointment product. During the analysis of stability samples Sciencetech modified the method by using an unapproved calculation to determine the Proteolytic Activity. The modified calculation was used instead of the approved calculation because the sample results were unexpectedly lower than the standard curve. While analyzing these same stability samples for Chlorophyllin Copper Complex Sodium, the customer's method was also modified when the optical reflectance was read at 465nm instead of the required 500nm. There is no assurance that these modifications did not affect the final results.
- 2) In addition to the examples of modifying both compendial methods and customer supplied methods, we also observed the use of unvalidated in-house analytical methods as well as unvalidated modifications to in-house methods. For example:
- a) While performing L-Lysine analyses for [REDACTED] Sciencetech's in-house method #1747 was used, however, the laboratory worksheets show that the diluent was changed and that a C18 column was used instead of the specified Amino column. These changes were not validated.
- b) Method #1747 was also used to perform Pre-Protein analyses for [REDACTED]. The method was modified again, in that a C8 column was used instead of the specified Amino column. The change was not validated.
- c) Sciencetech method #1742 was used to analyze [REDACTED] Syrup for [REDACTED]. Not only was the injection volume changed from 15ul to 5ul without reason, but the method had not been validated for the assay of Brompheniramine Maleate and Hydrocodone Bitartrate in combination with Guaifenesin. The method was developed for the assay of Chlorpheniramine Maleate and Hydrocodone Bitartrate.

A statement indicating that the method had not been validated in the particular formulation was included on the certificates of analysis for the L-Lysine, Pre-Protein, and [REDACTED] samples. Use of this statement does not absolve Sciencetech Laboratories from using valid, accurate, and reproducible methods. Sciencetech remains responsible for following established analytical methods exactly as they are written unless appropriate change control procedures have been followed.

- 3) The documentation practices at the North Branch facility were found to be insufficient and incomplete. These practices did not allow for comprehensive laboratory investigations, nor were they sufficient to determine the actual method employed for a specific analysis. For example:

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- a) Our investigator documented nine samples that were analyzed for Organic Volatile Impurities for [REDACTED]. None of the laboratory worksheets indicated which specific OVI method was followed. In addition, four of the sample worksheets did not show any record of chromatographic conditions.
 - b) A sample of [REDACTED] was analyzed for [REDACTED] according to the USP procedure, however, the laboratory worksheet did not document the appropriate heating of the sample, nor the creation of a standard curve necessary to calculate the amount of Free Ethylene Oxide in the sample.
 - c) Dimethyl Sulfoxide was analyzed for [REDACTED] as per the USP monograph. The sample failed several criteria and an investigation was performed. The investigation indicated that all analytical work was satisfactory, however, the laboratory worksheet for the Congealing Temperature test does not show all of the temperature recordings during testing, nor does it show the average of four temperature readings that fall within a range of 0.2° as required by the USP. A thorough and meaningful investigation cannot occur without complete documentation of the sample analysis.
- 4) The general laboratory practices that were observed and documented were unsatisfactory. For example:
- a) Expired reagents and test solutions continued to be available for use in the laboratory. These reagents and test solutions have not been shown to be suitable for use since they are only evaluated for odor, color, and appearance prior to being re-certified for use. No evaluation of the stability of these materials has been made beyond the expiration dates assigned by the manufacturers. For example, the following were observed in the laboratory:
 - Alizarin Red S: expiration date 1/81, recertified until 6/00
 - Glucono-Delta Lactone UG (lot 5V-77-15):
dated 10/89, recertified until 12/00
 - M-cresol Purple 0.1% (Lot 2122-5):
dated 5/94, recertified until 12/00
 - Ammonium Carbonate Test Solution:
prepared 7/99, expiration 1/00, available for use 5/00
 - b) Our review of Sciencetech's records showed deficiencies related to the secondary review of analytical data and calibration data. Specifically, method modifications, failure to record chromatographic conditions, mislabeled chromatograms, failing calibration data, and failure to perform specified testing on laboratory water were observed by our investigator but were not noted by any Sciencetech personnel performing secondary reviews of this data.

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- c) The recording chart shows that the humidity for the accelerated stability chamber was out of range from 2/9-10/00. This chamber had a specification of 75% Relative Humidity, +/-5%. No qualification data was available for the chamber, and there was no documentation showing that the problem had been investigated, repaired, or even reported to management.

The above list of violations is not considered to be all-inclusive of the violations at your facility. It is your responsibility to ensure that all requirements of the Federal Food, Drug and Cosmetic Act and all applicable federal regulations are met. Federal agencies are advised of the issuance of all Warning Letters about drugs and devices so that they may take this information into account when considering the award of contracts.

We have documented violations similar to those listed above during our inspections of 5/91, 5/94, 7/96, 8/97, 8/98, and 12/99. Our records show that corrective actions have been outlined in the past, yet we continue to see the same type of violations being repeated. You should now take prompt action to correct these deficiencies. Failure to correct the deviations may result in regulatory action without further notice. This includes seizure and/or injunction.

Please notify this office within 15 working days of receipt of this letter regarding the specific steps you have taken to correct the noted violations. This should also include an explanation of each step taken to prevent the recurrence of similar violations. If the corrective actions cannot be completed within 15 working days, state the reason for the delay and the time needed to complete the corrections.

Please submit your response to: U.S. Food and Drug Administration, 10 Waterview Boulevard, 3rd Floor, Parsippany, New Jersey 07054, Attn: Sarah A. Della Fave, Compliance Officer.

Sincerely,



Douglas I. Ellsworth
District Director
New Jersey District