



DEPARTMENT OF HEALTH AND HUMAN SERVICES

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Food and Drug Administration
New Orleans District
Nashville Branch Office
297 Plus Park Blvd.
Nashville, TN 37217

Telephone: 615/781-5380
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October 22, 2003

VIA FEDERAL EXPRESS
NEXT DAY DELIVERY

Mr. Kendred A. Young, Owner
Tri-State Analytical Laboratory LLC
71 Wilson Avenue
Johnson City, Tennessee 37604

Warning Letter No. 2004-NOL-03

Dear Mr. Young:

During an inspection of your facility on July 23-25, 2003, our investigator documented violations of the Current Good Manufacturing Practice Regulations (CGMP), Title 21, *Code of Federal Regulations*, Part 211. These violations cause the drug products that you analyze to be adulterated within the meaning of Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act).

The inspection revealed:

1. Analytical results were reported to [REDACTED] stating that a sample met specifications when either out-of-specifications (OOS) results were obtained on the sample analysis or on the quality control samples used to determine the validity of the analytical results. These OOS results were not investigated/documented properly to assure results reported to [REDACTED] were accurate and valid. [21 CFR 211.165(a)]
2. Inadequate method validation in that OOS findings were discarded without investigating the cause of the OOS results and analytical data was selectively reported to support the validation. [21 CFR 211.165(e)]
3. Use of reference standards and reagent solutions for extended periods of time without data in the analytical records supporting time of use. [21 CFR 211.194(c)]
4. Inadequate Standard Operating Procedures that are not always available, lack appropriate details, or contain contradictory information. For example, the written procedure for method validation lacks detailed instructions and acceptance criteria for each test and conflicts with the protocol. Additionally, some software application and microbiology lab autoclave procedures have not been validated adequately. [21 CFR 211.160(b)]

The above identification of violations 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 CGMP Regulations and to correct the violations noted in this letter and the Form FDA 483 issued at the conclusion of the inspection.

We acknowledge your response of August 6, 2003 to our investigator's observations noted on the Form FDA 483. We welcome your commitment to perform proper OOS investigations in the future and re-validate analytical methods, as well as other actions. However, the response was inadequate in some respects, including the following:

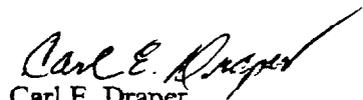
1. Your response appears to indicate the data reported to [REDACTED] in the past was appropriate, even though you acknowledge failures to perform formal OOS investigations to justify invalidating OOS results. OOS results cannot be invalidated without a proper investigation. For example, we would not agree that repeating Continuous Calibration Standard samples (essentially an accuracy sample) is a suitable means of invalidating an OOS result.
2. Your response states that raw data for some of the unreported method validation OOS results indicated there were assignable causes to justify not reporting the data (specifically for testing on January 3, 2003). However, these were not the only OOS results which were not reported in the validation packages (or which were not invalidated). Your response suggests that some of the unreported data cited on the Form FDA 483 was actually method development rather than validation; it appears to suggest this was the case for the testing done on January 3, 2003. However, data from January 3, 2003 (and from prior test runs) was reported in validation reports. You failed to identify (during the inspection or in your response) which data is method development and which data is validation, and how we could identify each of them.

You should take prompt action to correct these violations. Failure to correct these deviations promptly may result in regulatory action such as an injunction without further notice.

You should notify this office in writing within fifteen (15) working days of receipt of this letter of the specific steps, you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations.

If corrective action cannot be completed with fifteen (15) working days, state the reason for the delay and the time within which the corrections will be completed. Your reply should be directed to the attention of Joseph E. Hayes, Compliance Officer, Food and Drug Administration, 297 Plus Park Boulevard, Nashville, Tennessee 37217.

Sincerely,


Carl E. Draper
Director, New Orleans District

Enclosure: 21 CFR Part 211