



Food and Drug Administration
Kansas City District
Southwest Region
11630 West 80th Street
Lenexa, Kansas 66214-3340

Telephone: (913) 752-2100

May 18, 2004

**CERTIFIED MAIL
RETURN RECEIPT REQUESTED**

WARNING LETTER

Ref. KAN 2004-11

Dr. Richard M. Schwarz, Ph.D.
Chief Executive Officer
Custom Industrial Analysis Laboratories, Inc.
1717 Commercial St.
P. O. Box 3022
St. Joseph, MO 64503

Dear Dr. Schwarz:

During an inspection of your contract testing laboratory, conducted February 25 – March 3, 2004, an investigator and analysts from this office documented deviations from the Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals (Title 21, Code of Federal Regulations (CFR), Parts 210 & 211). These violations cause the drug products tested at your facility to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). The deviations from 21 CFR Part 211 include:

Failure to establish and document the accuracy, sensitivity, specificity, and reproducibility of test methods employed by the firm. [21 CFR 211.165(e)]

For example, the assay method for products containing tolinaftate (anti-fungal powder with tolinaftate 1% and [REDACTED]) has not been validated to show that the method used in the testing of the samples meet proper standards of accuracy and reliability as applied to the product tested and as stated in the firm's method CIA-140, "Assay for Tolinaftate Content."

Failure to follow approved analytical procedures for human and veterinary pharmaceutical drug testing, and failure to document and justify deviations from written sampling plans and test procedures. [21 CFR 211.160(a)]

For example, the testing method for Ethanol in OraTest, SOP LM-032-original, describes purging the column by increasing the temperature to 150 degrees C and holding for 10 minutes prior to the next injection. Testing of samples CIA Labs #

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126276, 126589, and 126590 dated February 7, 2004 recorded an initial column temperature of 90 degrees C and a final temperature of 90 degrees C. The temperature was not increased to 150 degrees C to purge the column. The justification for deviating from the method was not documented.

Other examples of deviations from written sampling plans and test procedures for human or veterinary pharmaceutical products include, but are not limited to:

- [REDACTED] powder and [REDACTED] Gel
- Ammonium Chloride Tablets 200 mg and 400 mg
- [REDACTED]
- [REDACTED]
- [REDACTED] 1% Spray
- [REDACTED]
- Pyrimethamine USP

Failure to conduct and document a thorough investigation of any unexplained discrepancy or failure of a batch to meet its specifications or extend the investigation to other batches that may have been associated with the specific failure or discrepancy. [21 CFR 211.192]

Your firm has demonstrated a pattern of failure to follow an adequate out-of-specification (OOS) procedure. OOS test results were noted for human or veterinary pharmaceutical products and were not sufficiently investigated. Examples of deviations include, but are not limited to the testing of the following products:

- Full Strength Pure Pork Thyroid Powder
- Amikacin Sulfate Injection
- Polyox (Magnesium Hydroxide) Powder
- Propylparaben
- Ammonium Chloride Powder
- Hydrogen Peroxide

For example, during an investigation for OOS results for Full Strength Pure Pork Thyroid Powder, CIA Lab # 120098 dated January 21, 2003, a digestion problem was suspected from a testing result with an unacceptable T4/T3 ratio. The sample was re-prepared in duplicate and confirmed the original results (unacceptable ratio). Samples were again re-prepared in duplicate, with acceptable T4/T3 ratio. These last acceptable results were averaged and reported. The specific cause was not determined. The first three results were disregarded as suspected problems from digestion, sample

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preparation, and/or standards. There was insufficient data to demonstrate conclusively that the initial results were incorrect. In addition, an investigation was not conducted to determine whether other samples were affected by problems with the methods, and there is no record of what was done to prevent these problems from recurring. OOS investigation of Full Strength Pure Pork Thyroid Powder, CIA Lab # 120096, CIA Lab # 120099, and CIA Lab # 120100 are additional examples of inadequate investigations.

Failure to maintain complete laboratory records that include a statement of each method used in the testing of a sample. [21 CFR 211.194(a)(2)] Laboratory records reviewed during the inspection failed to include information pertaining to:

- identification of mobile phase and/or solution
- identification of raw data/chromatograms
- statement of conformance to specifications
- statement of actual analytical method used
- identification of actual reviewing personnel

For example, the analysis data sheets for Full Strength Pure Pork Thyroid (CIA Labs # 120099 dated January 21, 2003) as well as the Certificate of Analysis for Full Strength Pure Pork Thyroid (CIA Labs # 120098 signed February 10, 2003), reference the method used as USP 26, p. 1830-1831. The actual method used for testing was an in-house method different from the USP method stated in the above mentioned documentation.

We acknowledge receipt of your response, dated March 15, 2004, to the Form FDA 483 issued at the close of the inspection. The promised corrective actions may not be adequate to correct all the deviations. In 2000 and 2001, your firm promised corrections after FDA reported inspectional findings and still the same deficiencies were noted during this inspection. Your facility is a contract testing laboratory that should be providing accurate, precise test results for its human and veterinary drug manufacturing clients. The CGMP deviations noted during this and the previous inspections indicate a chronic failure of the firm's quality system. Having the Quality Assurance unit be more diligent in the review of assay documentation and increasing the scrutinization of method documentation is important, but it does not address the underlying issue of the analysts performing the work. Adherence to your established standard operating procedures (SOPs) is essential for proper documentation of the work performed. Failure to follow your SOPs is evidenced by the treatment of OOS results on a case-by-case basis rather than following the SOP - Procedure C-3, which establishes criteria for reanalysis and data evaluation. Not following SOPs indicates a failure to assure that personnel have the necessary experience in, and a thorough understanding of, the operations that they perform.

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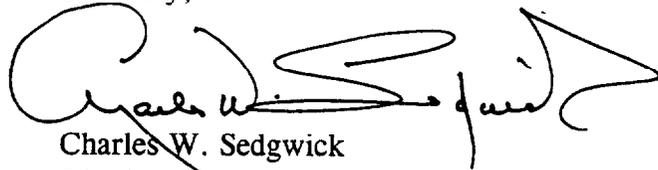
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This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure that your firm adheres to all requirements of the Act and its implementing regulations. Compliance with CGMPs is dependent on having control systems in place and minimizing, if not eliminating, process variations. You should know that these serious deviations may result in FDA taking regulatory action, such as seizure and/or injunction, without further notice to you.

Please submit, in writing, within fifteen working days of receiving this letter, your responses to the deviations identified in this letter. Your letter should include a description of the status of the corrective actions outlined in your March 15, 2004 letter. Your reply should be sent to Nadine Nanko Johnson, Compliance Officer, at the above address.

Sincerely,

A handwritten signature in black ink, appearing to read "Charles W. Sedgwick", written over a horizontal line.

Charles W. Sedgwick
District Director
Kansas City District