Inspections, Compliance, Enforcement, and Criminal Investigations

Earlham College 29-Jul-02

Department of Health and Human Services Public Health Service

Food and Drug Administration
Detroit District
1560 East Jefferson Avenue
Detroit, MI 48207-3179

Telephone: 313-226-6260
WARNING LETTER
2002-DT-32
RETURN RECEIPT REQUESTED
July 29, 2002

Douglas Bennett
President
Earlham College
801 National Road, West
Richmond, IN 47374

Dear Mr. Bennett:

Investigator Jeffrey A Sommers conducted an inspection of the Earlham Analytical Laboratory, operating within the Chemistry Department at your college, dated May 17-31, 2002. At the conclusion of the inspection Investigator Sommers issued a FORM FDA-483, list of Inspectional Observations (copy attached), to Ms. Mary A. Hagerman, Director-of the laboratory.

The inspection reported the laboratory is performing analytical testing for a drug manufacturing firm in serious violation of the Federal Food, Drug, and Cosmetic Act (the Act). Our investigator documented numerous significant deviations from the Good Manufacturing Practice Regulations, Title 21, Code of Federal Regulations (CFR), Part 211, which cause the prescription products, (Prenatal Vitamins and/or Minerals with Folk Acid, and Iron formulations) to be adulterated within the meaning of section 501(a)(2)(B) of the Act as follows:

1. (FORM FDA-483 Item #1)Failure to establish a Quality Control Unit with written procedures for the laboratory operations regarding the testing of drug products, as required by CFR 211.22.

2. (FORM FDA-483 Item #10)Failure to document training of the only laboratory person involved in drug testing as to specific methodology, instruments used, and the Current Good Manufacturing Practices (cGMP?s) relevant to laboratory operation as required by 21 CFR 211.25.

3. Failure to comply with the General Requirements of Subpart I. Laboratory Controls, as required by 21 CFR 211.160, in that there is:

a. (FORM FDA-483 Item #3) No validation of the test method for analysis of [redacted] for the in-process materials and finished dosage forms supplied by the contracting manufacturer.
b. (FORM FDA-483 Item #4)No verification that the test method using HPLC for Folk Acid analysis, following changes made by the laboratory from the official USP compendium method, is suitable for conditions of use in the testing of the contracting manufacturer?s in process and finished dosage forms.
c. (FORM FDA-483 Item #7)No established procedure for the usage of prepared standards solutions for testing folic acid and iron, and no data to support the stability of standards in solutions for up to one year after preparation.
d. (FORM FDA-483 Item #8) No provisions for receiving samples for testing, sample storage, time-frames for testing, or retention of remaining samples after analysis.
e. (FORM FDA-483 Item #9) No documentation of the quantity of samples received for testing, to include a description with the product name and batch or lot number.
f. (FORM FDA-483 Item #11) No established written program for the maintenance and calibration of instruments such as the atomic absorption and HPLC instruments and the [redacted] balance used for drug analysis.
g. (FORM FDA-483 Item #12) No certification to a recognized standard for the weights set used for checking the [redacted] balance.
h. (FORM FDA-483 Item #13) No established procedure for the qualification of analytical instruments for drug testing, when purchased and installed in this laboratory.
i. (FORM FDA-483 Item #15) No appendices existed that were referenced in the methods for testing folk acid in the two products, Vitaroca and Vinatal, that had been changed concerning the quantity of methanol used in the procedure.
j. (FORM FDA-483 Item #16) No current Standard Operating Procedures (SOP?s) had been established for laboratory operations prior to May 20, 2002.

4. (FORM FDA-483 Item #6) Failure to establish written procedures for the determination of system suitability for the HPLC test method of folk acid assay as required by the Testing and Release for Distribution requirements of Subpart I, Laboratory Controls of 21 CFR 211.165.

5. Failure to comply with the Laboratory Records requirements of Subpart J. Records and Reports, as required by 21 CFR 211.194 in that:

a. (FORM FDA-483 Item #14) There is no provision in the test method procedure for the use of an [redacted] spreadsheet for entering test parameters and calculation of test results that was used to calculate the results of blend samples of Vitaroca and

Vinatal from 5/6-13/02.

b. (FORM FDA-483-item #17) Worksheets are not always complete as to recorded data such as sample weights, final dilutions, and analyst initials or signature.

c. (FORM FDA-483 Item #18) There is no provision for review of test data and results prior to final release to the customer as a Certificate of Analysis Report.

d. (FORM FDA-483 Item #19) There was no documented investigation or justification for re-test of a blend sample # 11517-2G that was rerun on 5/13/02, due to not using the initial reading that was performed on 5/10/02.

e. (FORM FDA-483 Item #20) No investigation performed as to overlapping chromatographic peaks during the HPLC testing for folic acid in Vitaroca Plus blend samples in May 2002, including reruns of samples without any justification.

We request that you take prompt action to correct these violations. Failure to promptly correct these violations may result in enforcement action being initiated by the Food and Drug Administration without further notice, such as seizure and/or injunction.

In addition to the above listed violations, our Investigator noted that the laboratory is using an electronic record system for processing and storage of data from the atomic absorption and HPLC instruments that is not set up to control the security and data integrity in that the system is not password controlled, there is no systematic back-up provision, and there is no audit trail of the system capabilities. The system does not appear to be designed and controlled in compliance with the requirements of 21 CFR, Part 11, Electronic Records.

Please notify this office in writing, within fifteen (15) working days of receipt of this letter, as to any additional steps you have taken to correct these violations, including an explanation of each step being taken to identify and make corrections to assure that similar violations will not recur.

If corrective action cannot be completed within 15 working days, state the reason for the delay and the time frame within which the corrections will be implemented.

We suggest that you thoroughly evaluate the adequacy of your procedures and controls, and that you take whatever actions are necessary to make systemic corrections and to assure that similar violations will not recur. The above list of deviations is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to assure adherence to each requirement of the Good Manufacturing Practice Regulations. Other Federal agencies are advised of the issuance of all Warning Letters about drugs so that they may take this information into account when considering the award of contracts. Additionally, pending NDA, ANDA or export approval requests may not be approved until the above violations are corrected.

Your reply should be directed to Melvin 0. Robinson, Compliance Officer, at the above address.

Sincerely,

/s/

David M. Kaszubski for Joann M. Givens

District Director

Detroit District