DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
4040 North Central Expressway, Suite 300 Dallas, TX 75204 (214) 253-5200 Fax:(214) 253-5314 Industry Information: www.fda.gov/oc/industry	06/05/2013 - 06/17/2013* FEI NUMBER 3004549631

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED

TO: Ms. Toya N. Francis, Laboratory Manager

FIRM NAME	STREET ADDRESS
Eagle Analytical Services	9881 S Wilcrest Dr
CITY, STATE, ZIP CODE, COUNTRY	TYPE ESTABLISHMENT INSPECTED
Houston, TX 77099-5130	Contract Testing Laboratory

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM WE OBSERVED:

LABORATORY CONTROLS

OBSERVATION 1

Laboratory controls do not include the establishment of scientifically sound and appropriate specifications, standards, and test procedures designed to assure that components conform to appropriate standards of identity, strength, quality and purity.

Specifically,

A) There is no validation performed on the Rapid Scan RDI instrument to determine its suitability for use as a sterility test for product that they test.

B) Your firm does not conduct growth promotion on the Trypticase Soy Broth (TSB) and Fluid Thioglycollate Medium (FTM) used in their membrane filtration and direct inoculation sterility tests for drug product as required in the USP <71> Sterility test

C) There is no suitability testing performed on drug product samples prior or concurrently during membrane filtration sterility testing as required in the United States Pharmacopeia Chapter <71> Sterility Tests.

D) . Your firm does not indicate the number of samples received or required for sterility testing. USP <71> specifies the number of articles to be tested. While you provide reference to USP <71> for sample sizes, you do not ensure that your clients are submitting the required number of articles for testing.

E) Your firm has not validated your "plate contamination method" to determine whether it is suitable for its intended use by the customer as a sterility test method.

F) Your firm does not conduct growth promotion on the Tryptic Soy Agar plates used in testing drug product samples for microbial contamination via the TSA (Tryptic Soy Agar) Microbial Plating method.

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G) Finished product samples tested for microbial contamination using the Tryptic Soy Agar Microbial Plating Method were not tested for suitability to neutralize preservative interference and/or inhibition if present in finished product.

H) Certificates of Analyses of commercially purchased media used to test drug products for sterility tests (Trypticase Soy Broth and Fluid Thioglycollate) and Microbial plate contamination test using Tryptic Soy Agar are not maintained.

I) Your firm does not calculate the Maximum Valid Dilution (MVD) for finished product samples that are tested for bacterial endotoxins as required in the United States Pharmacopeia <85> Bacterial Endotoxins Test. MVD is the maximum allowable dilution of a product at which the endotoxin limit can be determined.

J) Your firm does not calculate endotoxin limits for drug product samples and therefore, cannot determine if finished product samples have more than the allowable endotoxin limit as required in the USP <85> Bacterial Endotoxins Test.

K) Your firm does not test pH for drug product samples tested for bacterial endotoxin as required in USP Chapter <85> Bacterial Endotoxins Test

L) Your firm has failed to Validate the Test Method for any potency assays conducted by your firm. You have not determined the evaluation of accuracy, sensitivity, specificity, and reproducibility of the test methods used in the analyses of drug products submitted by clients to your firm. Your firm routinely conducts analyses by HPLC per USP method of drug products to include: Vitamin D3, Thiamine HCL, Thioctic Acid, Methylcobalamine.

M) Your firm does not perform System Suitability for any HPLC analyses conducted on samples.

OBSERVATION 2

Deviations from written specifications are not justified.

Specifically,

A) 31 out or 33 Drug product samples were released as were tested for sterility on the SCAN RDI instrument on March 21, 2013. A typical run consists of Quality Control C3

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beads, drug product samples, one positive control and one negative control. The positive control used for the run was *Staphylococcus aureus.* It was run but it was not detected by the machine. Drug product samples that were run on March 21, 2013 via Rapid Scan RDI were passed and released even though the positive control was not recovered or out of specification. No documentation of this deviation was recorded except the printout of results for that day. The SOP for Rapid Scan RDI Quality Control #45B, dated 02/22/11 requires an OOS investigation for a failed control. There was no documentation of an investigation, and the results were released with the positive control with no growth. There was no positive control sample included 02/15/2013, and 03/22/2013. Additionally, the positive controls for 03/20/2013, and 06/19/2012 also had postive control with no microbial recovery/no growth.

OBSERVATION 3

Laboratory records do not include complete data derived from all tests, examinations and assay necessary to assure compliance with established specifications and standards.

Specifically,

A) The Sterility Tracking Logs and the Contamination Test Tracking Logs that your firm uses to record the placement of samples on sterility/plating testing in Incubators #1 and #2 are not maintained. All sterility and TSA Microbial Plating (formerly) samples are incubated by the firm in these two incubators by temperature. The incubator logs are the raw data for each sample placed in the incubator, interim observations (3, 7, and 14 days for sterility) and final test results. The records could only be located for approximately 4 months (January to April 2013) of samples analyzed by the firm. According to your Microbiologist Assistant Manager, the records were not maintained prior to this time period.

B) The Reference Standards used in the Potency Assay of Vitamin D sample ID 264253, 268952, and 271216 was not documented in the sample analysis records.

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OBSERVATION 4

Laboratory records do not include the initials or signature of a second person showing that the original records have been reviewed for accuracy, completeness, and compliance with established standards.

Specifically,

A) The Sterility Tracking Logs and Contamination Test Tracking Logs (TSA Microbial Plating Records) that were only available from approximately January 2013 through March 2013, do not have any signature for review. According to management, these records were not maintained until the start of January 2013.

B) The annual requalification records of the HPLCs #1069, 1071, and #1073 were not signed by management to indicate review and approval of the requalification.

QUALITY SYSTEM

OBSERVATION 5

There is no quality control unit.

Specifically,

Your firm failed to establish an effective Quality Control Unit (QCU) that has responsibility and authority for approving rejecting all procedures, methods, and specifications related to the identity, strength, quality, and purity of drug products submitted to your firm for analysis, and for reviewing laboratory records to assure that no errors had occurred or, if errors had occurred, that they have been fully investigated. Additionally, your firm has not developed any procedures describing these responsibilities.

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OBSERVATION 6

Written records are not made of investigations into unexplained discrepancies and the failure of a batch or any of its components to meet specifications.

Specifically,

A.) Your firm has no SOP on how to handle Out Of Specifications (OOS) results of any Sterility, Endotoxin, Tryptic Soy Agar Microbial Plate Contamination and Potency failures.

B.) Your firm has not conducted OOS investigations for your firm's analyses for any possibility of laboratory error, control sample issues, etc. For example:

1. Sample # 280479 (Ascorbic Acid) was analyzed by your firm on 03/21/2013 using Rapid ScanRDI for sterility determination. The data for this day indicates the positive control failed in that no microbial contamination was detected. There was no investigation for this failure. This same sample #280479 was reported as a sterility failure with 1"Event" reported. Additionally, Rapid Scan RDI data for 03/20/2013 and 06/19/2012 reported no growth for the positive control. There was no investigation.

2. Potency OOS reported by your firm include: Sample #271216 -Vitamin D3 assay results were reported as 13.8% potency, Sample # 264253 - Vitamin D3 assay results werer reported as 212% potency, Sample #263680 - Thioctic Acid assay results were reported as 39.2%. There was no investigation for these OOS.

OBSERVATION 7

Appropriate controls are not exercised over computers or related systems to assure that changes in master production and control records or other records are instituted only by authorized personnel.

Specifically,

Your firm has no control or security of your electronic records. The database used by your firm (Lab Light) to receive sample requests, assign sample numbers, and report sample results can be accessed and changed by any firm employee. The sample numbers generated by Lab light can be deleted as was demonstrated during this inspection. Additionally, the electronic

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software (Empower) used to manage your analytical lab equipment such as HPLCs, and UHPLCs does not have any security measures in place. For example: Any technician can access any analysis being run on the six liquid chromatography stations. Additionally, the ability to manually integrate the peaks is accessible to any technician before the particular assay is set to complete.

OBSERVATION 8

GMP training is not conducted on a continuing basis to assure that employees remain familiar with CGMP requirements applicable to them.

Specifically,

Your firm does not adequately train laboratory personnel. For example: staff performing bacterial endotoxin test indicate they were not trained in the principles and methodologies of the test and could not determine appropriate endotoxin limits for products under test.

* **DATES OF INSPECTION:**
06/05/2013(Wed), 06/06/2013(Thu), 06/07/2013(Fri), 06/10/2013(Mon), 06/11/2013(Tue), 06/12/2013(Wed), 06/14/2013(Fri), 06/17/2013(Mon)

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The observations of objectionable conditions and practices listed on the front of this form are reported:

1. Pursuant to Section 704(b) of the Federal Food, Drug and Cosmetic Act, or

2. To assist firms inspected in complying with the Acts and regulations enforced by the Food and Drug Administration

Section 704(b) of the Federal Food, Drug, and Cosmetic Act (21 USC 374(b)) provides:

"Upon completion of any such inspection of a factory, warehouse, consulting laboratory, or other establishment, and prior to leaving the premises, the officer or employee making the inspection shall give to the owner, operator, or agent in charge a report in writing setting forth any conditions or practices observed by him which, in his judgement, indicate that any food, drug, device, or cosmetic in such establishment (1) consists in whole or in part of any filthy, putrid, or decomposed substance, or (2) has been prepared, packed, or held under insanitary conditions whereby it may have become contaminated with filth, or whereby it may have been rendered injurious to health. A copy of such report shall be sent promptly to the Secretary."