U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Toxin Technology, Inc. 2/8/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
555 Windertey Pl., Ste. 200
Maitland, FL 32751

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WARNING LETTER

FLA-11-17

February 8, 2011

Raoul F. Reiser
President & RO
Toxin Technology, Inc.
7165 Curtiss Avenue
Sarasota, Florida 34231

Dear Dr. Reiser:

During our August 9 - 10, 2010 inspection of your active pharmaceutical ingredient (API) contract testing laboratory, Toxin Technology, Inc., located at 7165 Curtiss Avenue, Sarasota, Florida, investigators from the Food and Drug Administration (FDA) identified significant deviations from Current Good Manufacturing Practice (CGMP) for the manufacture of APIs. These deviations cause your client's API(s) to be adulterated within the meaning of section 501 (a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, CGMP.

We acknowledge your written responses, dated September 9, 2010, and October 11, 2010, to the Form FDA 483. However, because these responses were received more than 15 business days after the Form FDA 483 was issued, they have not been considered.[1] We plan to evaluate your response to the Form FDA 483, along with any other written material provided, as a direct response to this Warning Letter.

Specific deviations observed during the inspection include, but are not limited, to the following:

1. Your firm's Quality Unit failed to assure that materials are appropriately tested and the results are accurately reported.

For example, in numerous instances, your firm reported passing results after failing results were obtained. Examples include but are not limited to: (1) a result of 0.620 obtained for SPL #10-572, but reported by your firm as 0.156; (2) a result of 0.488 obtained for SPL #10-573, but reported by your firm as 0.105, and; (3) a result of 0.290 was obtained for SPL #10-1326, but your firm reported a test result of 0.190. Absorbance results > 0.200 are out-of-specification (OOS) results.

In addition, your firm's quality unit failed to report accurate results to your client. A comparison between the raw data and the reported results for several **(b)(4)** Pancrelipase samples revealed numerous documentation errors (e.g., SPL #10-590).

2. Failure to appropriately validate your analytical method.

For example, protocols were not developed and the validation study of Bacillus Diarrheal Entertoxin (BDE) using **(b)(4)** and **(b)(4)** methods was incomplete.

3. Failure to have a procedure to investigate and document, at the time of performance, OOS test results.

Your firm failed to investigate numerous OOS test results. Moreover, your firm lacked a written procedure for investigating OOS test results.

4. Failure to appropriately qualify analytical equipment used for BDE testing.

For example, since 2007, your firm has failed to calibrate the **(b)(4)** readers on a **(b)(4)** basis, as described in the operation manual for these instruments. These plate readers are used in the BDE-**(b)(4)** analysis.

5. Failure to have test records readily available during the retention period at the establishment where testing occurred or in a location where the records can be promptly retrieved by electronic or other means.

For example, your firm failed to locate raw data records for approximately 150 Pancrelipase samples tested fo BDE using the BDE-**(b)(4)** method between April 27, 2010 and July 29, 2010. Consequently, there was no ra test data available to show that the testing had been conducted. The reason given for why these records were missing -- an employee purportedly took these records home and could not locate them -- is wholly inadequate.

6. Failure to have personnel qualified by education, training, experience, or a combination thereof, to ensure that APIs are manufactured in accordance with CGMP.

Based upon the deviations described above (e.g., releasing numerous incorrect results to a client and the inability to locate original raw data sheets for approximately 150 samples), it appears that your firm's personnel lack a fundamental understanding of CGMP or have not been trained to perform their duties in accordance with CGMP.

As a contract laboratory that tests drugs, your firm is responsible for complying with CGMP. In addition, it is essentia that your firm provide all test results for evaluation and consideration by the owner of the product to consider in its final disposition decision. Please see FDA's Guidance for Industry entitled "Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Production" (October, 2006).

The deviations detailed in this letter are not intended to be an all-inclusive statement of deviations that exist at your facility. You are responsible for investigating and determining the causes of the deviations identified above and for preventing their recurrence and the occurrence of other deviations. It is your responsibility to assure compliance wit all requirements of federal law and FDA regulations.

You should take prompt action to correct the deviations detailed in this letter. Failure to promptly correct these deviations may result in legal action without further notice including, without limitation, an injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates or approval of pending drug applications listing your facility until the above deviations are corrected. FDA may re-inspect to verify corrective actions have been completed.

If you believe that your September 9, 2010 and October 11, 2010 written responses to the Form FDA 483 fully explai the actions you have taken to prevent similar violations in the future, please communicate that belief to us in writing within fifteen (15) working days. As noted above, we plan to evaluate your written responses along with any other written material provided as a direct response to this Warning Letter. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction. Additionally, your response should state if you no longer test API(s) at this facility, and provide the date(s) and reason(s) you ceased testing.

Your reply should be sent to the attention of: Winston R. Alejo, Compliance Officer, Food and Drug Administration 55 Winderley Place, Suite 200, Maitland, Florida 32751. If you have questions regarding any issues in this letter, please contact Mr. Alejo at (407) 475-4731.

Sincerely,

/s/

Emma R. Singleton
Director, Florida District

cc: **(b)(6)**
(b)(4)

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[1] 74 Fed. Reg. 40211-12 (Aug. 11, 2009).

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