U.S. Department of Health & Human Services

U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Synbiotics Ltd

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring MD 20993

Warning Letter

VIA UPS MAIL

WL: 320-11-06

December 16, 2010

Mr. Kartikeya Sarabhai
Chairman
Synbiotics Limited c/o Ambalal Sarabhai Enterprises
Shanti Sadan, Mirzapur Road, near Janasatta Press
Ahmadabad 380 001
India

Dear Mr. Sarabhai:

On August 23, 2010, the U.S. Food and Drug Administration arrived at Synbiotics Limited, your manufacturing facility for active pharmaceutical ingredients (API), located at Plot Nos. 570, 571, 576A, Maitry Marg, Village-Luna, Tal Padra (Dt.), Vadodara, India, to conduct an inspection. Your firm denied our investigator access into the facility, and instead requested that the investigator remain in a business office located at Asence Pharma Private Ltd., Parshwa Pooja Complex, Akota, Vadodara, India. During August 23-27, 2010, information and limited documents provided to the investigator for review revealed significant deviations from Current Good Manufacturing Practice (CGMP) for the manufacture of APIs. These deviations cause your 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 have reviewed your firm's response of September 1, 2010, and note that it lacks sufficient corrective actions.

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

1. Failure to prepare, review, and approve documents related to the manufacture of APIs.

For example, you shipped Lot **(b)(4)** of **(b)(4)**, to the United States in January 2010 from this site. At the time of shipment, no procedures were in place for change control, out-of-specification investigations, process deviation investigations, laboratory incidents, consumer complaint handling, or annual product reviews. Without these and other basic CGMP procedures in place, there is minimal assurance of appropriate systems to assure product quality.

Your response acknowledges that your quality system "was inadequate" and that "critical Quality Assurance functions were missing." Your response also includes SOPs, covering topics such as change control, out of specification results, deviation control, market complaints and product quality reviews, which were specifically requested during the August 2010 inspection attempt. It is your responsibility to ensure these and other critical procedures and essential quality assurance functions are in place prior to manufacturing. Your quality system will be thoroughly reviewed during the next FDA inspection.

2. Failure of your quality system to provide confidence that your API manufacturing processes will consistently yield a product meeting its intended specifications.

For example, at the time of shipment of the above-referenced lot of **(b)(4)**, you had not performed validation of the manufacturing process for **(b)(4)**, nor had you established a process design, a validation plan, or qualification protocols. Process validation is essential to establish initial and ongoing reproducibility of your manufacturing operation. Furthermore, process validation is expected before commercial distribution begins. Without an adequate validation plan or written procedures to execute pre-defined qualification protocols, your manufacturing process can not be confirmed as being capable of reliable commercial manufacturing that consistently delivers a product that meets its pre-defined quality attributes.

Your response acknowledges that you have not completed process validation for the **(b)(4)** process used to manufacture Lot **(b)(4)**. It is our expectation that process validation be complete prior to commercial distribution. Additionally, your response states that Lot **(b)(4)** met USP requirements at its release and again during retain re-testing and because the product meets the USP requirements, "this batch is completely safe and there are no quality issues." FDA disagrees with this statement as you have already acknowledged that process validation has not yet been completed at the time of Lot **(b)(4)**'s manufacture and that your quality system "was inadequate" and that "critical Quality Assurance functions were missing."

In response to this letter, provide the timeline by which your facility will be ready for re-inspection, accounting for process validation, essential procedures being in place, critical quality functions established, and training.

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. If you wish to continue to ship APIs to the United States, it is the responsibility of your firm to ensure compliance with all U.S. standards for CGMP and all applicable U.S. laws and regulations.

Until all corrections have been completed and FDA has confirmed corrections of the deviations and your firm's compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as an API manufacturer. In addition, failure to correct these deviations may result in FDA refusing admission of articles manufactured at Synbiotics Limited, Plot Nos. 570, 571, 576A, Maitry Marg, Village-Luna, Tal Padra (Dt.), Vadodara, India into the United States. The articles are subject to refusal of admission pursuant to section 801(a)(3) of the Act [21 U.S.C. § 381(a)(3)] in that the methods and controls used in their manufacture do not appear to conform to Current Good Manufacturing Practice within the meaning of section 501(a)(2)(B) of the Act [21 U.S.C. § 351(a)(2)(B)].

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct deviations. Include an explanation of each step being taken to prevent the recurrence of deviations and copies of supporting documentation. 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. Please identify your response with FEI # 3008494993.

If you have questions or concerns regarding this letter, contact Brian Belz, Compliance Officer, at the below address and telephone number.

U.S. Food and Drug Administration
Center for Drug Evaluation and Research
Division of Manufacturing and Product Quality
International Compliance Branch
White Oak, Building 51
10903 New Hampshire Ave
Silver Spring, MD 20993
Tel: (301) 796-4279
Fax: (301) 847-8741

Sincerely,
/S/
Richard L. Friedman
Director
Division of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research

Links on this page: