U.S. Department of Health & Human Services

U.S. Food & Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Labor L+S AG 12/15/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring MD 2099

Warning Letter

VIA UPS MAIL

WL: 320-12-07

December 15, 2011

Dr. Lothar Bomblies
Member of the Board
Labor L+S AG
Mangelsfeld 4
Bad Bocklet-Grossenbrach
Germany D-97708

Dear Dr. Bomblies:

During our July 18-21, 2011 inspection of your contract testing laboratory facility, Labor L+S AG, located at Mangelsfeld 4, Bad Bocklet-Grossenbrach, Germany, an investigator from the Food and Drug Administration (FDA) identified significant violations of Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211. These violations cause drugs tested by your facility 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 August 2, 2011, and note that it lacks sufficient corrective actions.

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

1. Your firm has not thoroughly investigated any unexplained discrepancies or the failure of a batch or any of its components to meet its specification whether or not the batch has been distributed [21 C.F.R. 211.192].

For example, your firm's investigations associated with Internal Deviation Reports, 2227 (02/15/2010), 2243 (02/23/2010), 2293 (03/01/2010), 2789 (10/20/10), 3226 (03/25/2011), and 3427 (06/06/2011), for missing environmental samples and failure to perform complete finished product testing are deficient. These deviation reports were approved by your Quality Unit.

Your investigation into these incidents concluded that these errors occurred "inadvertently." However, the investigation failed to establish a root cause and your quality unit failed to ensure the implementation of adequate corrective actions to prevent future recurrence.

In addition, the investigator found several Internal Deviation Reports in which you did not identify the products involved or the final test results associated with these investigations.

You indicated in your response that the deviation reports were reassessed by senior management together with Quality Assurance. Your response is inadequate because you did not describe how you conducted the reassessment or include the procedure that you followed, you failed to establish root cause after the reassessment, and you did not provide documented evidence indicating approval by your Quality Unit.

Your response also states that you have implemented a plan to reassess all deviations and Out-of-Specification (OOS) results from 2009, 2010, and 2011 by October 1, 2011.

In your response to this letter please provide; 1) a summary report of your reassessment of all deviations and OOS results from 2009 to present including a description of each investigation that you have conducted, the nature of the OOS, with the root cause and corrective actions; 2) evidence that all your customers were notified of these failures/deviations and provide the dates of notifications; 3) the specific corrective actions taken to improve your program for handling deviations, including adequate training to assure competencies of all personnel; and 4) your current procedure for deviation investigations, including how your firm responds when adverse trends are observed.

2. Your firm allowed inadequately trained and unqualified personnel to perform sterility tests in the **(b)(4)** and clean room [21 C.F.R. § 211.25 (a)].

For example, the inspection revealed that one of the sterility testing technicians conducted sterility testing unsupervised in January 2010 prior to completing analytical testing training (February 4, 2010) as required by your training procedure L+S SOP-1.009.

Although this technician's training record contained a remark by the Division Director that the technician was released for sterility testing under supervision on December 23, 2009, your records contain no indication that this operator was being supervised while conducting sterility testing on January 12, 13, 14, 25, 27, and 28, 2010.

In your firm's response, you indicated that you are in the process of revising your training program and you provided a timeline for its completion. In addition, you indicated that, during the last few years, your firm was aware of the inadequacies of the training program established in 2000, yet failed to address them. Your response is inadequate because you failed to assess your training program to determine the analysts that could have been impacted or to evaluate the testing performed by these analysts trained since 2000.

In your response to this letter please include a description of your revised training program, including how you will improve your assessment of training effectiveness, and any other corrective actions implemented to prevent recurrence.

Please note that it is a requirement of CGMP that your firm have a robust quality system providing for adequate investigations, to include sustainable corrective and preventive actions and trending and appropriately trained personnel.

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility. You are responsible for

investigating and determining the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations. If you wish to continue to test pharmaceutical components or drug products intended for distribution in 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. To ensure proper evaluation of your responses, please reply in English, including all attachments.

Until all corrections have been completed and FDA has confirmed corrections of the violations and your firm's compliance with CGMP, FDA may withhold approval of any new applications or supplements listing your firm as a contract testing laboratory. In addition, failure to correct these violations may result in FDA refusing admission into the United States of articles tested at Labor L+S AG, located at Mangelsfeld 4, Bad Bocklet-Grossenbrach, Germany. 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 (15) working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations and copies of supporting documentation. If you cannot complete corrective action within fifteen (15) 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 # 3002807481.

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

U.S. Food and Drug Administration
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Sincerely,

/Steven Lynn/
Acting Director
Office of Manufacturing and Product Quality
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