Inspections, Compliance, Enforcement, and Criminal Investigations

CBSCHEM LIMITED 1/31/14

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Silver Spring, MD 20993

Warning Letter

WL: 320-14-02

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

January 31, 2014

Kamran Malik
President
CBSCHEM Limited
Unit 1303, 13th Floor, Block 4
18 Tin Hua Road
Nan Fung Industrial City
Tuen Mun, New Territories, Hong Kong

Dear Mr. Kamran Malik:

During our April 24, 2013, and June 3 through June 7, 2013 inspections of your pharmaceutical labeler/relabeler facilities, CBSCHEM Limited, 621 S 48th St., Suite 114, Tempe, AZ 85281-2325 USA, and CBSCHEM Limited located at Unit 1303, 13th Floor, Block 4, 18 Tin Hua Road, Nan Fung Industrial City, Tuen Mun, New Territories, Hong Kong, investigators from the U.S. Food and Drug Administration (FDA) identified significant deviations from current good manufacturing practice (CGMP) for the labeling/relabeling of active pharmaceutical ingredients (APIs). These deviations cause your APIs 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.

In addition, these APIs are misbranded pursuant to Section 502(a) of the Act [21 U.S.C. 352(a)] and Section 502(i)(1) of Act [21 U.S.C. 352(i)(1)].

We have conducted a detailed review of your firm's response for the facility in Hong Kong and note that it lacks sufficient corrective actions.

Our investigators observed specific violations during the inspections of your sites, including, but not limited to, the following:

A. CBSCHEM Limited, Nan Fung Industrial City, Tuen Mun, New Territories, Hong Kong

1. Failure to maintain complete records for your APIs.

a. You did not retain records for the complete traceability for the APIs distributed by your firm. For example, our inspection found that records for 23 lots of APIs did not contain the batch numbers, manufacturing dates, and expiration or retest dates. We also observed inconsistent record retention practices with regard to the original manufacturer including the manufacturer's identity, address, batch number, purchase, receipt, transportation, distribution, and Certificates of Analysis (COAs). The inspection found lots of **(b)(4)**, and **(b)(4)** lots of **(b)(4)** listed in your records of inventory did not have this information.

b. Your inventory records did not contain sufficient information to identify and track the APIs received by, and distributed from CBSChem Limited. For example, records for **(b)(4)** and **(b)(4)** APIs did not contain invoice numbers. As such, your firm was unable to provide receipt and distribution records for these APIs.

Your response is inadequate because you do not provide sufficient detail regarding how you will maintain and control appropriate records to ensure supply chain reconcilability of your APIs. You also do not identify personnel or the work units responsible for these activities. In your response to this letter, provide a detailed procedure for control and retention of your CGMP related records.

Please note that the guidance document entitled "Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients" (ICH CGMP guidance), describes current good manufacturing practice (CGMP) for the manufacture and distribution of APIs. Section 17.2, Agents, Brokers, Traders, Distributors, Repackers, and Relabellers, *Traceability of Distributed APIs and Intermediates* describes in detail records that ensure the traceability of your products. The ICH Q7 guidance may be accessed at the following internet link:
http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073497.pdf[1]

2. Failure to transfer all quality or regulatory information received from the API manufacturer to your customers.

Your firm's COAs lacked the identity of the original manufacturer of the API and the actual testing facility. In addition, it is essential that a COA include batch or lot codes, laboratory testing information, expiry or retest dates, and other relevant information.

You provided no response to this deviation. In your response to this letter, provide written procedures for the transfer of quality and

regulatory information to your customers. Include how you will ensure the information is accurate and complete. Provide specific details of the information you will transfer, and how you will transfer it to your customers, most notably through creating an adequate COA.

3. Failure to control the API repackaging, relabeling, and holding operations in order to avoid mix-ups and the loss of the API identity.

For example,

a. Your firm's practice of storing unlabeled APIs inside inadequately labeled totes can lead to mix-ups.

b. You did not segregate returned APIs; instead you stored them on the same shelves as incoming APIs without clear separation or identification.

Your response is inadequate because you do not provide sufficient detail of your corrective actions. You do not describe your quarantine procedure to prevent mix-ups, identification and labeling procedures, or how you will approve or reject materials. In your response to this letter, provide detailed written procedures addressing these deficiencies and describe how your firm will ensure that these procedures are properly implemented.

4. Failure to have a Quality Unit responsible for reviewing and approving CGMP documents and procedures, and assuring product quality.

During the inspection, you stated you did not have a quality unit, provided no written documents describing the roles and responsibilities of a Quality Unit, and had no written procedures for quality activities.

Your response indicates that you will make corrective actions but does not provide adequate detail. In response to this letter, provide a written procedure for your quality unit that should include, but not be limited to the following quality oversight activities: approving or rejecting all APIs, packaging and labeling materials; reviewing completed batch and laboratory control records before determining if an API lot can be released; ensuring that discrepancies, complaints, returns, and failures are investigated and resolved; approving all specifications; approving all procedures affecting the quality of APIs: approving raw material vendors, API contract manufacturers, contract laboratories, and other outsourced activities; approving changes that potentially affect API quality for their acceptability; making sure that materials are appropriately tested and the results are reported; making sure that there is stability data to support retest or expiry dates and storage conditions of your APIs.

B. CBSCHEM Limited, Tempe, AZ, USA

1. Failure to relabel and hold APIs under appropriate CGMP controls.

FDA's inspection of your facility determined that a container labeled as **(b)(4)**(an excipient) did not contain **(b)(4)**. In fact, FDA's testing of the contents of the container identified different ingredients including **(b)(4)** (used to treat **(b)(4)**), **(b)(4)** (used to treat **(b)(4)**), **(b)(4)** (used to treat **(b)(4)**), **(b)(4)** (used to treat **(b)(4)**), and **(b)(4)** (used to treat **(b)(4)**). The unacceptable practices that resulted in this mislabeling incident can pose a severe hazard to consumers.

2. Failure to maintain complete records for APIs.

Your firm failed to implement a quality system to ensure the identity of your APIs. More specifically, your firm failed to provide basic documents that must be retained including those with the identity and address of the original manufacturer (e.g., COAs, other records with critical information regarding the ingredients). In addition, your firm's COAs lacked the name, address, and telephone number of the original manufacturer and approval of the authorized quality unit personnel.

Misbranding Deviations

These active pharmaceutical ingredients are misbranded within the meaning of Section 502(a) of the Act [21 U.S.C. 352(a)] in that their labeling is false or misleading in any particular.

These active pharmaceutical ingredients are misbranded within the meaning of Section 502(i)(1) of the Act [21 U.S.C. 352(i)(1)] in that the active pharmaceutical ingredients and its containers are so made, formed, or filled as to be misleading.

The deviations cited in this letter are not intended to be an all-inclusive list 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.

The CGMP deviations listed in this letter as well as other deficiencies our investigators found, lead us to question the effectiveness of your current quality system to achieve overall compliance with CGMP at CBSCHEM Limited, Nan Fung Industrial City, Tuen Mun, New Territories, Hong Kong, and CBSCHEM Limited, Tempe, AZ. It is apparent that you have not implemented a robust quality system at your firm. Be advised that corporate management is responsible for ensuring the quality, safety, and integrity of APIs distributed by CBSCHEM Limited. FDA strongly recommends that your executive management immediately undertake a comprehensive evaluation of your global operations to ensure compliance with CGMP requirements.

Due to continuing CGMP issues at your firm, we recommend you engage a third party consultant with appropriate CGMP expertise to assess your firm's facility, procedures, processes, and systems to ensure that the APIs you distribute have their appropriate identity, strength, quality, and purity.

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 an API Labeler/Relabeler. In addition, your failure to correct these deviations may result in FDA continuing to refuse admission of articles distributed by CBSCHEM Limited located at Unit 1303, 13th Floor, Block 4, 18 Tin Hua Road, Nan Fung Industrial City, Tuen Mun, New Territories, Hong Kong into the United States under Section 801(a)(3) of the Act, 21 U.S.C. 381(a)(3). The articles may be 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 CGMP 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 and prevent the recurrence of deviations, and provide copies of supporting documentation. If you cannot complete corrective actions within fifteen working days, state the reason for the delay and the date by which you will have completed the

corrections. Additionally, if you no longer distribute the APIs at issue, provide the dates and reasons you ceased distribution. Please identify your response with FEI # 3008746159.

Your reply to the Warning Letter concerning CBSCHEM Limited, Nan Fung Industrial City, Tuen Mun, New Territories, Hong Kong facility should be sent to the Food & Drug Administration, Center for Drug Evaluation and Research, Office of Compliance, Office of Manufacturing and Product Quality, Division of International Drug Quality, White Oak Building 51, 10903 New Hampshire Avenue, Silver Spring, Maryland 20993, to the attention of Joseph Duran, Compliance Officer. In addition, your reply to the Warning Letter concerning CBSCHEM Limited, Tempe, AZ USA facility should be sent to the Food & Drug Administration, Los Angeles District Office, 19701 Fairfield, Irvine, CA, 92612, to the attention of John Stamp, Compliance Officer.

Sincerely,
/S/
Steven J. Lynn
Director
Office of Manufacturing and Product Quality

Page Last Updated: 02/06/2014
Note: If you need help accessing information in different file formats, see Instructions for Downloading Viewers and Players.

Links on this page:

1. http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073497.pdf