Inspections, Compliance, Enforcement, and Criminal Investigations

Posh Chemicals Private Limited 8/2/13

Department of Health and Human Services

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

Warning Letter

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

WL: 320-13-23

August 02, 2013

Mr. Surya Ratna Prasad Cherukuri
Managing Director
Posh Chemicals Pvt Ltd
202 S.V.'s Classic Residency, 6-3-853/2
Ameerpet
Hyderabad 500 016, India

Dear Mr. Cherukuri:

During our March 3-8, 2013 inspection of your pharmaceutical manufacturing facility, Posh Chemicals Private Limited, located at Unit II, Plot No. 23, Phase-1, Jeedimetla, Hyderabad, India, investigator(s) from the U.S. Food and Drug Administration (FDA) identified significant deviations from current good manufacturing practice (CGMP) for the manufacture 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.

We acknowledge receipt of your firm's correspondence dated April 1, 2013.

Our investigator(s) observed specific violations during the inspection, including, but not limited to, the following:

1. Failure to protect computerized data from unauthorized access or changes.

Our inspection found that there were no restrictions to access the laboratory data residing on the workstations attached to your standalone instrumentation: **(b)(4)** High Pressure Liquid Chromatographs (HPLCs), the Fourier Transform Infrared Spectrophotometer (FTIR), the gas chromatograph (GC) and the drives and portable media used as back-ups. There was no protection of the data from alteration and deletion and no audit trails to detect if such alteration or deletion had occurred. You have stated that you are in the process of purchasing and updating software to handle these problems. You have also stated that there had been no misconduct by laboratory personnel. However, our investigator uncovered misconduct by laboratory personnel (see issue 3 below). Please provide a detailed summary of your

investigations that led to the conclusion that no misconduct occurred. Also, please provide a description of your corrections, including system upgrades. This description should be detailed enough to determine if this deficiency has been addressed.

2. Failure to ensure that test procedures are scientifically sound and appropriate to ensure that key starting materials and intermediate(s) conform to established standards of quality and/or purity.

Your laboratory uses non-validated assays for testing of key starting materials and for an intermediate used in the manufacture of **(b)(4)** API. Please submit method validation reports to support the scientific validity of these methods. In addition, please submit the validation status of all other non-compendial analytical methods used in your laboratory along with a timeline for completing any necessary validation activities.

3. Failure to follow and document quality-related activities at the time they are performed.

During this inspection, your QC Chemist admitted that, under the direction of a senior colleague, he had recorded false visual examination data in the logbooks for reserve samples. This QC Chemist was responsible for multiple entries in the **(b)(4)** API logbooks. Your firm's failure to prevent, detect, and rectify the falsification of your GMP documentation is concerning. In response to this letter, describe your investigation into this misconduct and clearly explain how you determined the extent of the data falsification. Describe the role of the senior colleague who advised the QC Chemist during this incident. Also describe your plans for and outcome of a thorough investigation into data integrity at your facility, both in documents produced by the QC Chemist involved in this incident and by all other personnel at your site.

Our inspection also found that your laboratory failed to take note of a trend in the total impurity test results reported for this API. A striking number of the long term room temperature stability results show a drop in the total impurities result (for the most recent test) regardless of whether that is the 12, 24, 36, 40 or 48 month test interval.

The deviations pertaining to the APIs manufactured at your facility that are 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. You are also responsible for preventing their recurrence and the occurrence of other deviations.

You are also responsible for compliance with the regulations for finished pharmaceuticals under 21 CFR 210 and 211 when your manufacturing includes the combination of an API with an excipient, e.g., when **(b)(4)** is further processed for the US into an in–process material, **(b)(4)**.

If, as a result of receiving this warning letter or for other reasons, you are considering a decision that could reduce the number of finished drug products or active pharmaceutical ingredients produced by your manufacturing facility, FDA requests that you contact CDER's Drug Shortages Program immediately, as you begin your internal discussions, at drugshortages@fda.hhs.gov so that we can work with you on the most effective way to bring your operations into compliance with the law. Contacting the Drug Shortages Program also allows you to meet any obligations you may have to report discontinuances in the manufacture of your drug under 21 U.S.C. 356C(a)(1), and allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on your products. In appropriate cases, you may be able to take corrective action without interrupting supply, or to shorten any interruption, thereby avoiding or limiting drug shortages.

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 manufacturer. In addition, your failure to correct these violations may result in FDA refusing admission of articles manufactured at Posh Chemicals Pvt Ltd, Hyderabad, India 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 manufacture or distribute **(b)(4)**, the API at issue, provide the date(s) and reason(s) you ceased production. Please identify your response with FEI # 3001329340.

Please send your reply to: Regina T. Brown, Compliance Officer, Food and Drug Administration, CDER/OC/OMPQ/DIDQ/ICB1 Bldg. 51 Rm 4248, 10903 New Hampshire Avenue, Silver Spring, MD 20903.

Sincerely,
/S/
Michael D. Smedley
Acting Director
Office of Manufacturing and Product Quality
Office of Compliance
Center for Drug Evaluation and Research

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