U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

ChemPacific Corporation 4/7/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
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Central Region
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FEI# 3003299802

WARNING LETTER
CMS# 150412

April 7, 2011

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Dr. Chen Zhou, CEO
ChemPacific Corporation
6200 Freeport Center
Baltimore, MD 21224

Dear Dr. Zhou:

During our September 27-29 and October 1, 4-5, and 9, 2010 inspection of your active pharmaceutical ingredient (API) manufacturing facility, ChemPacific Corporation, located at 6200 Freeport Center, Baltimore, Maryland, 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 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 received your firm's response of November 9, 2010, and note that it lacks sufficient corrective actions.

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

1. Failure of your Quality Unit to record all quality-related activities at the time they are performed.

For example, your firm failed to complete batch records at the time the API was manufactured. Specifically, the manufacturing batch record for Norepinephrine Bitartrate (lots **(b)(4)**) contained incomplete or missing entries regarding the manufacturing operations performed. We are concerned with your practice of back-dating records and the inability of your quality unit to detect the problem.

Please note that batch records are critical records and it is your responsibility to ensure proper, accurate, concurrent, and authentic documentation of activities associated with each lot. The corrective actions in your response for this observation appear to be adequate (e.g., training employees on procedures, further review of additional batch records). However, although you have stated that you will review additional batch records, please indicate what actions you will take should this review reveal inaccurate, missing data, etc. in other batch records. Also, please provide in your response information regarding any other retrospective evaluation conducted to determine the extent of the problem (e.g., other employees that may not have been involved in the incidents described above) and impact on lots released for distribution.

2. Failure to document and/or retain equipment cleaning records.

For example, your firm failed to have records documenting the cleaning of containers used to store Norepinephrine Bitartrate (lots **(b)(4)**). Your firm was observed using containers to store intermediates without any prior cleaning.

In your response, your firm commits to reject these batches as an unqualified CGMP product. Your response, however, is not adequate because it does not address the practice of using unclean storage containers, nor does it describe your firm's proposed corrective action.

3. Failure to conduct an appropriate out-of-specification (OOS) laboratory investigation in accordance with written procedures.

For example, your firm failed to follow your OOS procedure to conduct an appropriate investigation when an OOS purity test result for Norepinephrine Hydrochloride identified high levels of Arternone impurities in the original sample. Specifically, your investigation failed to follow your procedures when your firm (1) initiated Phase 2 sample testing prior to completing Phase 1 of the investigation, and (2) only analyzed two samples as opposed to the required three samples.

In your response, your firm states that you have updated the procedures for OOS investigations and have provided additional training with the analysts. Your response, however, is inadequate because your OOS procedure states that you will invalidate OOS result following re-injection if they are in agreement with the original result (See Section 5.4.1 of your OOS procedure). This SOP is inadequate because the original OOS result should not be invalidated without a complete investigation to identify the assignable cause.

Please refer to the October 2006 Guidance for Industry-Investigating Out-of-Specification (OOS) Test Results for Pharmaceutical Products.

4. Failure to calibrate, in accordance with written procedures and an established schedule, weighing equipment critical for ensuring the quality of APIs.

For example, your firm failed to properly calibrate the **(b)(4)** scale **(b)(4)** within the range of its intended use. Although the **(b)(4)** scale was calibrated to 500mg (0.5g) and underwent daily verifications to 100mg (0.1g), the scale was used numerous times to determine laboratory sample weights as small as 10mg (0.01g).

In your response, your firm provided certification calibration records from your calibration services contractor to address actual use ranges of the balances. Your response, however, is inadequate because you do not include any information regarding a calibration program to ensure future calibration of balances on a routine basis.

The deviations cited 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 assur compliance with all requirements of federal law and FDA regulations.

You should take prompt action to correct the deviations cited in this letter. Failure to promptly correct these deviations may result in legal action without further notice including, without limitation, seizure and 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.

Your firm wrote Chinese characters which signified "need to change" on **(b)(4)** different batch records for **(b)(4)** lots **(b)(4)** of Norepinephrine Bitartrate. Although your Standard Operating Procedure (SOP) entitled "Documentation and Record Keeping Practices," indicates proper handling of errors (i.e., a single line through the error, notation of the correction, and inclusion of initials, current date, and the reason or explanation for the correction), an individual at your firm told our investigators that the characters indicated that these marked batch record pages were to be replaced with a corrected batch record page. In your response, your firr states that the **(b)(4)** batches will not be used for GMP purposes. Your firm also indicated that you have revised your SOP 04106 **(b)(4)**, "Batch Record issuance for **(b)(4)**," to require approval of the Vice President of Quality Assurance prior to the issuance of replacement pages and to issue these pages only in rare cases, and that in all cases the original pages will be maintained as part of the batch record and that any original entries will not be obliterated. Your response for this observatio is not adequate. Although you have not explained what rare cases would cause you to reissue replacement batch record pages, it is our view that blank duplicate batc record pages should not be issued for the purpose of re-writing a page to correct an error. The original document should be corrected as per your SOP.

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 send your reply to the U.S. Food and Drug Administration, Attention: Anne Aberdeen, Compliance Officer, 6000 Metro Drive, Suite 101, Baltimore, MD 21215. I you have questions regarding any issues in this letter, please contact Ms. Aberdeen at (410) 779-5134.

Sincerely,
/S/
Evelyn Bonnin
District Director
Baltimore District

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