WARNING LETTER

Asclemed USA Inc. dba Enovachem

MARCS-CMS 575542 — 11/06/2019

Delivery Method:

VIA SIGNATURE CONFIRMED DELIVE

Product:

Drugs

Recipient:

Mr. Robert Nickell

President/CEO/Owner

Asclemed USA Inc. dba Enovachem

379 Van Ness Ave, Suite 1403
Torrance, CA 90501
United States

Issuing Office:

Division of Pharmaceutical Quality Operations IV

19701 Fairchild
Irvine, CA 92612
United States

WARNING LETTER

VIA SIGNATURE CONFIRMED DELIVERY

June 11, 2019

Mr. Robert Nickell

President/CEO/Owner

Asclemed USA Inc. dba Enovachem

379 Van Ness Ave, Suite 1403

Torrance, CA 90501

Dear Mr. Nickell:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Asclemed USA Inc. doing business as Enovachem, FEI 3001452204, at 379 Van Ness Avenue, Suite 1403, Torrance, CA from September 25 to 27, 2018.

This warning letter summarizes significant deviations from current good manufacturing practice (CGMP) for active pharmaceutical ingredients (API).

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your API are adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

We reviewed your October 9, 2018, response in detail and acknowledge receipt of your subsequent correspondence.

During our inspection, our investigator observed specific deviations including, but not limited to, the following.

1. Failure to maintain complete traceability of API in commercial distribution.

For API you repackaged and distributed, you failed to obtain and retain documents with the identity of the original manufacturer and certificates of analysis (COA) from the original manufacturer.

Your response stated that you purchase API from a supplier, **(b)(4)**, also a repacker, that does not provide you the information of the original manufacturer. Your response, however, does not indicate how you intend to ensure full traceability of the supply chain, such as using only suppliers that provide the name of the original manufacturer, for the drugs you repackage.

In response to this letter, provide a retrospective review of drugs currently in distribution that are missing the required original manufacturer information from your suppliers.

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

You did not include the names and addresses of the original manufacturers of your repackaged API on COA you issued to your customers. For example, you did not include the manufacturer information on your COA for the opioid tramadol hydrochloride USP, testosterone USP (micronized), and estriol USP (micronized). You distributed these API with incomplete information to your customers, including pharmacies and physicians, for prescription compounding.

Your response is inadequate because you do not commit to ensure that your COA contain information about the original manufacturer.

Customers and regulators rely on COA for information about the quality and source of drugs and their components. Omitting information from the COA compromises supply chain accountability and traceability, and may put consumers at risk.

See *Guidance for Industry: Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* and *Q7 Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients—Questions and Answers* for more information on how API, from original manufacturers as well as API repackagers and relabelers, should be labeled and should clearly identify the original API manufacturer as the API moves through the supply chain. The

guidance documents can be found at: https://www.fda.gov/media/71518/download (https://www.fda.gov/media/71518/download) and https://www.fda.gov/media/112426/download (https://www.fda.gov/media/112426/download).

In response to this letter, provide the following:

- a remediated program for generating COA, including systems and procedures to assure that COA issued by your firm include necessary original manufacturer information;
- a retrospective review to determine how your failure to provide required information may have affected drug quality, and indicate any actions you have taken or will take, such as notifying customers, or invalidating previously issued COA for any drugs still within their labeled retest dates; and
- examples of recently-issued COA that include specific information regarding the original manufacturer, including a copy of their original batch certificate.

3. Failure to ensure that necessary calibrations are performed and recorded.

You failed to appropriately calibrate scales used to weigh API for their intended use. For example, scale 5 used to weigh small amounts of estriol API down to **(b)(4)** grams was calibrated at **(b)(4)**, and **(b)(4)** grams, which did not bracket the precise amount of API to be weighed. Additionally, the **(b)(4)**-gram weight used for scale verification checks was last calibrated in 2008.

Your response stated the use of the scales was halted and your policies were updated to include yearly weight calibration. However, your response did not indicate how you plan to review equipment calibration.

In response to this letter, provide the following:

- your review of product distributed that may have been affected by inadequate calibration of scales for intended use;
- your plan to notify customers affected by the inadequate scale calibration; and
- your corrective actions and preventive actions for routine management oversight of equipment to ensure prompt detection of equipment performance issues, execution of repairs, completion of preventative maintenance, and equipment calibration.

4. Failure to ensure regular quality reviews of API are conducted and documented annually.

You failed to have adequate records for periodic quality reviews of each drug. For example, your records included meeting attendees but did not include details on the information reviewed.

Your response stated that the periodic quality review summary and trending requested by the investigator would be “duplicating the review of the review… and to re-do a review at the end of the year.” However, your response does not support that you conducted a comprehensive annual product review of your drugs and procedures. Failure to perform annual product quality reviews limits your ability to verify the consistency of your repackaging processes, and to evaluate and assess whether corrective action or revalidation should be undertaken.

In response to this letter, provide the following:

- plan to ensure that you will complete, and document adequately, product quality reviews at least annually for all drug products; and
- procedures for investigating, responding to, and correcting any deviations from product quality and safety standards identified as a part of your product quality review findings and risk assessments.

CGMP consultant recommended

Based upon the nature of the deviations we identified at your firm, we strongly recommend engaging a consultant qualified to evaluate your operations to assist your firm in meeting CGMP requirements.

Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for resolving all deficiencies and systemic flaws to ensure ongoing CGMP compliance.

Concerns regarding glycerin

Your product list collected during the inspection included products containing glycerin. The use of glycerin contaminated with diethylene glycol (DEG) has resulted in various lethal poisoning incidents in humans worldwide. See FDA's guidance document, *Testing of Glycerin for Diethylene Glycol,* to help you meet CGMP requirements when distributing glycerin for use in drug products, including testing for DEG and recommendations for supply chain integrity, at https://www.fda.gov/media/71029/download (https://www.fda.gov/media/71029/download).

Conclusion

Deviations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these deviations, for determining the causes, for preventing their recurrence, and for preventing other deviations.

Correct the deviations cited in this letter promptly. Failure to promptly correct these deviations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved deviations in this warning letter may also prevent other Federal agencies from awarding contracts.

Until these deviations are corrected, we may withhold approval of pending drug applications listing your facility. We may re-inspect to verify that you have completed your corrective actions.

After you receive this letter, respond to this office in writing within 15 working days. Specify what you have done since our inspection to correct your deviations and to prevent their recurrence. If you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Send your electronic reply to ORAPHARM4_RESPONSES@FDA.HHS.GOV (mailto:ORAPHARM4_RESPONSES@FDA.HHS.GOV) or mail your reply to:

CDR Steven E. Porter, Jr.

Director, Division of Pharmaceutical Quality Operations IV

19701 Fairchild Road

Irvine, CA 92612

Please identify your response with unique identifier 575542.

If you have questions regarding any issues in this letter, please contact CAPT Matthew R. Dionne, Compliance Officer, at (303)-236-3064, or Matthew.Dionne@fda.hhs.gov (mailto:Matthew.Dionne@fda.hhs.gov).

Sincerely,

/S/

CDR Steven E. Porter, Jr.

Director, Division of Pharmaceutical Quality Operations IV

More Warning Letters (/inspections-compliance-enforcement-and-criminal-investigations/compliance-actions-and-activities/warning-letters)