Continental Manufacturing Chemist, Inc. 12/21/17

U.S. FOOD & DRUG ADMINISTRATION

Division of Pharmaceutical
Quality Operations III
300 River Place, Suite 5900
Detroit, MI 48207
Telephone: (313) 393-8100
Fax: (313) 393-8139

December 21, 2017

WARNING LETTER

Case# 532514

UPS NEXT DAY
SIGNATURE REQUIRED

Stuart H. Miller President/Owner
Continental Manufacturing Chemist, Inc.
(b)(6)

Dear Mr. Miller:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Continental Manufacturing Chemist, Inc., FEI 1910648, at 912 S. State St., Madrid, Iowa, from April 24 to 28, 2017.

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See 21 CFR, parts 210 and 211.

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products 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 May 12, 2017, response in detail.

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

1. Your firm failed to maintain adequate separate defined areas necessary to prevent contamination or mix-up (21 CFR 211.42(c)).

You manufacture several over-the-counter (OTC) drug products and medicated otic and oral care products under contract. These drugs include **(b)(4)** Ear Wax Drops, **(b)(4)** Oral Rinse, and fluoride toothpastes. You also manufacture numerous non-pharmaceutical materials in your facility, including a weed killer and adhesive remover.

You did not utilize any quarantine markings or physical segregation of finished drug products from the lawn care and cleaning chemicals in your warehouse. You did not designate your quarantined finished drug products with quarantined status. During the inspection, your Vice President of Operations stated that your firm does not quarantine any finished products before they are released by quality because you "thought of the product as good once it was manufactured."

Your response stated that your warehousing space is "tight," and you have recently acquired additional off-site space to store packaging components. You also stated that you would implement a procedure by July 1, 2017, for labeling the status of finished drug products.

Your response lacked sufficient detail on how you will ensure products are quarantined prior to release by the quality control unit. Furthermore, your response did not address the potential for product mix-ups in your storage facility or indicate how you separate pharmaceutical products from potentially toxic non-pharmaceutical products at your facility.

In your response to this letter, provide your plan to implement complete physical separation of pharmaceutical and non-pharmaceutical products and specify how you will implement controls to prevent product mix-ups among your pharmaceutical products.

2. Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging materials, labeling, and drug products (21 CFR 211.22(a)).

Your firm shipped finished products before your quality unit released the batches. For example, you distributed at least three batches of **(b)(4)** Oral Rinse and two batches of **(b)(4)** fluoride toothpaste without review of records and release by your quality unit.

In your response, you stated that you plan to:

- discontinue your procedure allowing shipment of your drugs before your quality unit releases the drugs;
- revise your procedure for release and review of your drugs; and
- perform a retrospective evaluation and risk assessment of products to determine whether products were properly held under quarantine prior to release.

Your response did not provide sufficient detail. You did not demonstrate that you have discontinued the practice of shipping prior to release or show how you will ensure that products are not shipped prior to release, e.g., by revising your shipping procedures to require your staff to verify and record confirmation that products have been released prior to shipping.

In response to this letter, submit your updated procedures, updated corrective actions, and the assessment of risk to patients for all products within the past three years that you shipped prior to release by your quality control unit.

3. Your firm failed to thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet any of its specifications, whether or not the batch has already been distributed (21 CFR 211.192).

Your quality control unit failed to thoroughly investigate at least 12 out of 16 discrepancies for issues ranging from product quality to customer complaints for contamination and faulty container closuresystems. You also failed to thoroughly investigate at least 8 out of 16 discrepancies related to manufacturing processes that occurred since September 19, 2014.

In your response, you state that you plan to:

- perform adequate risk assessments and close all discrepancy reports greater than two weeks old by June 3, 2017; and
- revise your procedure for handling customer complaints to include timeframes, complaint investigation methodology, and product risk assessment guidelines by September 1, 2017.

Your response was inadequate. You did not provide details on how you intend to close discrepancy reports going forward. You did not address your failure to investigate the non-conformances and deviations. You did not explain how you will ensure that complaints, discrepancies, failures, and process deviations will be thoroughly investigated and adequately documented in a timely fashion in the future. In addition, it is unclear whether your revised procedure includes the criteria for determining when an investigation is necessary. It is your responsibility to investigate complaints or document the reason when an investigation is not conducted.

4. Your firm failed to ensure that laboratory records included complete data derived from all tests necessary to assure compliance with established specifications and standards (21 CFR 211.194(a)).

Your firm did not keep laboratory records of sample preparations and analyses. Our investigator observed that during your laboratory analysis of Veterinary Liniment, lot

155476, your analysts did not record the method used, analytical steps performed, reagents used, the sample used, or which analyst prepared the sample.

Our investigator requested laboratory records of sample preparation and analyses for other drug products. Your Vice President of Operations stated in an affidavit that your firm could not provide these records because they do not exist. He stated that your lab analysts currently do not document their process of sample preparation for HPLC and GC testing.

In your response, you stated that you will train your employees on record keeping practices by May 26, 2017. You also stated that you will develop an interim procedure for proper record keeping practices and will issue laboratory notebooks and preparation worksheets by May 26, 2017.

Your response was inadequate. You did not assess the risks to patients and product quality posed by your failure to maintain complete laboratory records.

In response to this letter, summarize your efforts to ensure that your laboratory records include complete data for all laboratory tests. Include your risk assessment, revised procedures, and any other supporting documentation for your corrective actions.

Repeat violations

You have failed to correct repeat violations which have been observed in previous inspections and advisory actions from 2009–2014. Specifically, charges 1, 2, and 3 were repeat violations from a Regulatory Meeting held on May 13, 2010, as well as in an Untitled Letter dated November 27, 2013.

We acknowledge that you are using a consultant to audit your operation and assist in meeting FDA requirements. However, your executive management remains responsible for fully resolving all deficiencies, and ensuring ongoing CGMP compliance. You should immediately and comprehensively assess your company's manufacturing operations to ensure that systems and processes, and ultimately, the products manufactured, conform to FDA requirements.

Conclusion

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

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

Until these violations 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. We may also refuse your requests for export certificates.

After you receive this letter, respond in writing within fifteen (15) working days. Specify what you have done since our inspection to correct your violations 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.

Please send your electronic reply to**: ORAPHARM3_RESPONSES@fda.hhs.gov. (mailto:ORAPHARM3_RESPONSES@fda.hhs.gov)**

Attn:
Brian D. Garthwaite, Ph.D.
Compliance Officer
U. S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III

Refer to the Unique Identification Number (Case# 532514) when replying. If you have questions regarding the contents of this letter, please contact Dr. Garthwaite by phone at (612) 758-7132.

Sincerely,
/S/
Art O. Czabaniuk
Program Division Director
Division of Pharmaceutical Quality Operations III

cc:
Stephen B. DeMarcky
Vice President of Operations
Continental Manufacturing Chemist, Inc.
912 S. State Street
Madrid, IA 50156-1748

More in 2017 (/ICECI/EnforcementActions/WarningLetters/2017/default.htm)