RC Outsourcing LLC 11/28/17

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

November 28, 2017

WARNING LETTER

Case# 540511

UPS NEXT DAY
SIGNATURE REQUIRED

Raymond R. Carlson, Owner
RC Outsourcing, LLC
102 East Water St.
Lowellville, OH 44436-1117

Dear Mr. Carlson:

You originally registered with the U.S. Food and Drug Administration (FDA) as an outsourcing facility under section 503B of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353b]***[1]*** on October 6, 2015, and most recently on October 25, 2016. From March 27, 2017, to March 31, 2017, FDA investigators inspected your facility, RC Outsourcing, LLC, located at 102 East Water St., Lowellville, OH 44436-1117. During the inspection, the investigators noted serious deficiencies in your practices for producing sterile drug products, which put patients at risk.

FDA issued a Form FDA 483 to your facility on March 31, 2017. FDA acknowledges receipt of your facility's response, dated May 9, 2017, and your subsequent response, dated June 8, 2017. Based on this inspection, it appears you produced drugs that violate the FDCA.

A. Compounded Drug Products under the FDCA

The Drug Quality and Security Act (DQSA) was enacted on November 27, 2013. Title I of the DQSA, the Compounding Quality Act (CQA), added a new section 503B to the FDCA. Under section 503B(b) of the FDCA, a compounder can register as an outsourcing facility with FDA. Drug products compounded by or under the direct supervision of a licensed pharmacist in an outsourcing facility qualify for exemptions from the drug approval requirements in section 505 of the FDCA [21 U.S.C. § 355(a)], the requirement in section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] that labeling bear adequate directions for use and the Drug Supply Chain Security Act requirements in section 582 of the FDCA [21 U.S.C. § 360eee-1] if the conditions in section 503B of the FDCA are met.

An outsourcing facility, which is defined in section 503B(d)(4) of the FDCA [21 U.S.C. § 353b(d)(4)], is a facility at one geographic location or address that — (i) is engaged in the compounding of sterile drugs; (ii) has elected to register as an outsourcing facility; and (iii) complies with all of the requirements of this section. Outsourcing facilities must comply with other applicable provisions of the FDCA, including section 501(a)(2)(B) [21 U.S.C. § 351(a)(2)(B)], regarding current good manufacturing practice (CGMP), and section 501(a)(2)(A) [21 U.S.C. § 351(a)(2)(A)], regarding insanitary conditions. Generally, CGMP requirements for the preparation of drug products are established in Title 21 of the Code of Federal Regulations (CFR) parts 210 and 211.

Specific violations are described below.

B. Violations of the FDCA

Adulterated Drug Products

FDA investigators noted CGMP violations at your facility, that caused your drug product(s) to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA. The violations include, for example:

1. Your firm failed to establish and follow appropriate written procedures that are designed to prevent microbiological contamination of drug products purporting to be sterile, and that include validation of all aseptic and sterilization processes (Observations 3 and 5) (21 CFR 211.113(b)).

2. 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 (Observation 1) (21 CFR 211.192).

3. Your firm failed to establish an adequate system for monitoring environmental conditions in aseptic processing areas (Observation 6) (21 CFR 211.42(c)(10)(iv)).

Outsourcing facilities must comply with CGMP requirements under section 501(a)(2)(B) of the FDCA. FDA's regulations regarding CGMP requirements for the preparation of drug products have been established in 21 CFR parts 210 and 211. FDA intends to promulgate more specific CGMP regulations for outsourcing facilities. FDA has issued a draft guidance, *Current Good Manufacturing Practice — Interim Guidance for Human Drug Compounding Outsourcing Facilities under*

Section 503B of the FD&C Act. This draft guidance, when finalized, will describe FDA's expectations regarding outsourcing facilities and the CGMP requirements in 21 CFR parts 210 and 211 until more specific CGMP regulations for outsourcing facilities are promulgated.

Under section 301(a) of the FDCA [21 U.S.C. § 331(a)], the introduction or delivery for introduction into interstate commerce of any drug that is adulterated is a prohibited act. Further, it is a prohibited act under section 301(k) of the FDCA [21 U.S.C. § 331(k)] to do any act with respect to a drug, if such act is done while the drug is held for sale after shipment in interstate commerce and results in the drug being adulterated.

C. Corrective Actions

We have reviewed your facility's responses to the Form FDA 483.

Although some of your proposed corrective actions appear to be adequate, others appear to be deficient or could not be fully evaluated due to lack of adequate supporting documentation. For example, you state that you made changes to the "media challenge" process and submitted an updated SOP; however, your SOP does not include procedures for growth promotion testing of **(b)(4)** media used for the "high risk validation" procedure. In addition, you state that you have made changes to your SOP regarding alert and action levels and that you "have begun working on establishing a thorough investigative process and a complete follow up on such events"; however, you did not provide an SOP for instruction of media plate reading for review, and you did not provide documentation that training occurred to qualify operators to read and handle plates.

Your response to our observation of inadequate environmental monitoring of the aseptic processing area is deficient. Specifically, your firm's SOP P3.12.1.1 "Procedure-Testing-Environment-Sterile Environment," states that only "**(b)(4)** will be used **(b)(4)** during compounding for **(b)(4)**, and **(b)(4)**"; however, you do not monitor the fingertips of both hands. Also, you have not committed to daily volumetric viable air sampling, for example, with an active air sampler.

In addition to the issues discussed above, you should note that CGMP requires the implementation of quality oversight and controls over the manufacture of drugs, including the safety of raw materials, materials used in drug manufacturing, and finished drug products. *See* section 501 of the FDCA. If you choose to contract with a laboratory to perform some functions required by CGMP, it is essential that you select a qualified contractor and that you maintain sufficient oversight of the contractor's operations to ensure that it is fully CGMP compliant. Regardless of whether you rely on a contract facility, you are responsible for assuring that drugs you produce are neither adulterated nor misbranded. [*See* 21 CFR 210.1(b), 21 CFR 200.10(b).]

FDA strongly recommends that your management undertake a comprehensive assessment of operations, including facility design, procedures, personnel, processes, maintenance, materials, and systems. In particular, this review should assess your aseptic processing operations. A third-party consultant with relevant

sterile drug manufacturing expertise should assist you in conducting this comprehensive evaluation.

D. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations at your facility. You are responsible for investigating and determining the causes of the violations identified above and for preventing their recurrence or the occurrence of other violations. It is your responsibility to ensure that your firm complies with all requirements of federal law, including FDA regulations.

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

Within fifteen (15) working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct the violations. Please include an explanation of each step being taken to prevent the recurrence of the violations, as well as copies of related documentation. If you do not believe that the products discussed above are in violation of the FDCA, include your reasoning and any supporting information for our consideration. If you cannot complete corrective action within fifteen (15) working days, state the reason for the delay and the time within which you will complete the correction.

Please send your electronic reply to: ORAPHARM3_RESPONSES@fda.hhs.gov.

Attn: Tina M. Pawlowski, Compliance Officer
U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III

Refer to the Unique Identification Number (540511). If you have questions regarding the contents of this letter, please contact Tina M. Pawlowski by phone at (313) 393-8217.

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

---

[1] *See* Pub. L. No. 113-54, § 102(a), 127 Stat. 587, 587-588 (2013).