SCA Pharmaceuticals 6/25/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Dallas District Office
4040 North Central
Expressway
Suite 300
Dallas, Texas 75204

June 25, 2015

2015-DAL-WL-19

WARNING LETTER

UPS OVERNIGHT

Roy Eugene Graves, Chief Executive Officer
SCA Pharmaceuticals, LLC
8821 Knoedl Court
Little Rock, AR 72205-4600

Dear Mr. Graves:

You 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 December 13, 2013, and again on December 22, 2014. From March 17 to April 1, 2014, FDA investigators inspected your facility, SCA Pharmaceuticals, Inc., located at 8821 Knoedl Court, Little Rock, AR 72205-4600. During the inspection, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, the investigators observed that your firm failed to perform adequate investigations of sterility failures, batches found to contain particulates, and daily pressure differentials that were out-of-specification. Investigators also observed that your firm does not perform adequate environmental monitoring of the ISO 5 areas or endotoxin testing on all your sterile drug products. In addition, the investigators observed that you failed to meet the conditions under section 503B of the FDCA necessary for drugs produced by an outsourcing facility to qualify for exemptions from certain requirements under the FDCA. FDA issued a FDA 483 to your facility on April 1, 2014. FDA acknowledges receipt of your facility's response, dated April 22, 2014. FDA also acknowledges your action in January 2015 to voluntarily recall two lots of Glycopyrrolate Injection, 1 mg/5 mL Syringes, which were labeled with an expiration date that was unclear.

Based on this inspection, it appears your facility is producing drugs that violate the FDCA.

A. Compounded Drugs 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), 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 can 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 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.

B. Violations of the FDCA

FDA investigators observed significant CGMP violations at your facility, causing your drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA.

In addition, the FDA investigators observed that your facility failed to meet the conditions of section 503B. For example, during the inspection, the FDA investigators noted:

1. Some of your facility's drug products do not include the following statements on the label: "This is a compounded drug," "Not for resale," and the following information on the container to facilitate adverse event reporting: **www.fda.gov/medwatch** and 1-800-FDA-1088 (section 503B(a)(10) of the FDCA [21 U.S.C. §353b(a)(10)]).

2. Your facility failed to submit a report to FDA in December 2013 and in June 2014 identifying the drug products that you compounded during the previous 6-month period (section 503B(b)(2) of the FDCA [21 U.S.C. §353b(b)(2)]).

Because your compounded drug products have not met all of the conditions in section 503B, they are not eligible for the exemptions under section 503B from the FDA approval requirements in section 505, the requirement under section 502(f)(1) that labeling bear adequate directions for use, and the Drug Supply Chain Security Act requirements described in section 582 of the FDCA. ***[2]*** In addition, the mislabeled drug products that you distributed and subsequently recalled are also misbranded under section 502(a) of the FDCA [21 U.S.C. § 352(a)].

Specific violations are described below.

Adulterated Drug Products

FDA investigators noted CGMP violations at your facility, causing your drug products 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 thoroughly investigate any unexplained discrepancy or failure of a batch or any of its components to meet its specifications, whether or not the batch has already been distributed (21 CFR 211.192).

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

3. Your firm does not have, for each batch of drug product purporting to be sterile and/or pyrogen-free, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product (21 CFR 211.167(a)).

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.

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.

Misbranded Drug Products

You compound drug products that are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners; therefore adequate directions for use cannot be written so that a layman can use these products safely for their intended uses. Consequently, their labeling fails to bear adequate directions for their intended uses, causing them to be misbranded under section 502(f)(1) of the FDCA, and they are not exempt from the requirements of section 502(f)(1) of the FDCA (*see, e.g.,* 21 CFR 201.115).

In addition, in January 2015, you voluntarily recalled two lots of Glycopyrrolate Injection, 1 mg/5 mL Syringes, which were labeled with an unclear expiration date. A printing error caused an overlap in the "y" and "3," making the actual "Use By 3/2015" date on the drug product labels appear to read "Use By 8/2015." Under section 502(a) of the FDCA, a drug product is misbranded if its labeling is false or misleading in any particular. Because the labeling of these drug products was false, they are misbranded under section 502(a) of the FDCA.

It is a prohibited act under section 301(k) of the FDCA 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 misbranded.

Failure to Report Drugs

As noted above, your facility failed to submit a report to FDA upon initial registration as an outsourcing facility in December 2013 and again in June 2014, identifying the drug products that you compounded during the previous 6-month period (section 503B(b)(2) of the FDCA [21 U.S.C. § 353b(b)(2)]). The failure to report drugs by an entity that is registered with FDA in accordance with section 503B(b) is a prohibited act under section 301(ccc)(3) of the FDCA [21 U.S.C. § 331(ccc)(3)].

C. Corrective Actions

In your April 22, 2014, response to the Form FDA 483 you described certain corrective actions you took in response to the Form FDA 483 observations. Although several of your proposed corrective actions appear adequate, others are deficient. For example, your written response stated that you have "invested in new equipment in order to perform the **(b)(4)** sterility testing." However, your plan is to use this equipment only to "facilitate the root causes of sterility failures that would lead to adequate corrective/preventive actions, follow-up (verification) and conclusions throughout the entire facility" and not as your primary test method for sterility testing. Your firm has not shown that the sterility test method routinely used for release is adequate for its intended use. In addition, you stated that you plan to perform air monitoring and work surface sampling on a **(b)(4)**. It is not clear if your firm intends to perform air monitoring during dynamic conditions and work surface sampling immediately following production.

FDA strongly recommends that your management immediately undertake a comprehensive assessment of your operations, including facility design, procedures, personnel, processes, materials, and systems. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant sterile drug manufacturing expertise could be useful in conducting this comprehensive evaluation. You should fully implement necessary corrections in order to ensure that the drug products produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

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. FDA intends to re-inspect your facility to verify corrective actions have been completed.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps you have taken to correct violations. Please include an explanation of each step being taken to prevent the recurrence of 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 the corrective actions cannot be completed within fifteen working days, state the reason for the delay and the time frame within which the corrections will be completed. Your written notification should refer to the Warning Letter Number above (2015-DAL-WL-19). Please address your reply to Rose Ashley, Compliance Officer, at the address above.

If you have questions regarding the contents of this letter, please contact Rose Ashley at (210) 308-1407.

Sincerely,
/S/
Reynaldo R. Rodriguez, Jr.
Dallas District Director

cc:

John Clay Kirtley, Pharm.D
Executive Director
Arkansas State Board of Pharmacy
322 South Main Street, Suite 600
Little Rock, AR 72201

Nathanial Smith, MD, MPH
Director, State Health Officer
State of Arkansas Department of Health
4815 West Markham Street
Little Rock, Arkansas 72205

---

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

[2] See, e.g., section 503B(a)(11) of the FDCA [21 U.S.C. § 353b(a)(11)].