FDA U.S. FOOD & DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS

VIA UNITED PARCEL SERVICE
SIGNATURE REQUIRED

March 27, 2019

Ms. Karen L. Muir
Pharmacist-in-Charge
Safeway, Inc.
dba Safeway Compounding Pharmacy
6100 Hellyer Avenue, Ste 100
San Jose, CA 95138-1057

Dear Ms. Muir:

From June 5, 2017, to June 12, 2017, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Safeway, Inc., dba Safeway Compounding Pharmacy, located at 6100 Hellyer Avenue, Ste 100, San Jose, CA 95138-1057. During the inspection, the investigators noted that drug products you produced failed to meet the conditions of section 503A of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353a] for exemption from certain provisions of the FDCA.

FDA issued a Form FDA 483 to your firm on June 12, 2017. FDA acknowledges receipt of your facility's responses, dated June 26, 2017, and January 10, 2018, as well as your subsequent correspondence. Based on this inspection, it appears your firm is producing drugs that violated the FDCA.

A. Compounded Drug Products Under the FDCA

Section 503A [21 U.S.C. § 353a] of the FDCA describes the conditions under which human drug products compounded by a licensed pharmacist in a state licensed pharmacy or a federal facility, or a licensed physician, qualify for exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) [section 501(a)(2)(B)]; labeling with adequate directions for use [section 502(f)(1)]; and FDA approval prior to marketing (section 505) [21 U.S.C. §§ 351(a)(2)(B), 352(f)(1) and 355(a)].[1] Receipt of valid prescriptions for individually-identified patients is one of the conditions for the exemptions under section 503A.

In addition, for a compounded drug product to qualify for the exemptions under section 503A, bulk drug substances used to compound it must: (I) comply with the standards of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (II) if such a monograph does not

[1] We remind you that there are conditions other than those discussed in this letter that must be satisfied to qualify for the exemptions in section 503A of the Act.

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exist, be components of drugs approved by the Secretary; or (III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appear on a list developed by the Secretary through regulations ("503A bulks list")(section 503A(b)(1)(A)(i) of the FDCA).

B. Failure to Meet the Conditions of Section 503A

During the inspection, FDA investigators noted that drug products produced by your firm failed to meet the conditions of section 503A of the FDCA [21 U.S.C. § 353A]. Specifically, the investigators noted that your firm compounded drug products using (b) (4) . Drug products compounded using (b) (4) are not eligible for the exemptions provided by section 503A(a), because this bulk drug substance is not the subject of applicable USP or NF monographs, is not a component of FDA-approved human drugs, and does not appear on the 503A bulks list.[2]

Therefore, you compounded drug products that do not meet the conditions of section 503A of the FDCA and are not eligible for the exemptions from the FDA approval requirement of section 505 of the FDCA, the requirement under section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)] that labeling bear adequate directions for use, and the requirement of compliance with CGMP under section 501(a)(2)(B) of the FDCA [21 U.S.C. § 351(a)(2)(B)]. In the remainder of this letter, we refer to your drug products that do not qualify for exemptions under section 503A of the FDCA as the "ineligible drug products."

Specific violations are described below.

C. Violations of the FDCA

Adulterated Drug Products

During the inspection, the FDA investigators observed that drug products intended or expected to be sterile were prepared, packed, or held under insanitary conditions, whereby they may have become contaminated with filth or rendered injurious to health, causing your drug products to be adulterated under section 501(a)(2)(A) of the FDCA. For example, the investigators

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[2] In January 2017, FDA issued a revised final guidance titled, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. This guidance describes FDA's interim regulatory policy for State-licensed pharmacies, Federal facilities, and licensed physicians that compound human drug products using bulk drug substances that do not otherwise meet the conditions of section 503A(b)(1)(A)(i) while the 503A bulks list is being developed. Specifically, the guidance sets out the conditions under which FDA does not intend to take action against a State-licensed pharmacy, Federal facility, or licensed physician for compounding a drug product using a bulk drug substance that is not the subject of an applicable USP or NF monograph or a component of an FDA-approved drug, until the substance is identified in a final rule as included or not included on the 503A bulks list. These conditions include that the substance may be eligible for inclusion on the 503A bulks list, was nominated with adequate support for FDA to evaluate it, and has not been identified by FDA as a substance that appears to present significant safety risks pending further evaluation. (b) (4) was nominated for inclusion on the 503A bulks list; however, it was not nominated with adequate support for FDA to evaluate the substance. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf. For a list of bulk drug substances that have been nominated for use in compounding under section 503A, see https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/PharmacyCompounding/UCM467373.pdf.

observed that your aseptic processing areas were deficient in that walls were not smooth and hard surfaces were difficult to clean. In addition, your firm performed environmental sampling after cleaning, which could potentially bias the results. Furthermore, your firm failed to confirm that the quality of (b) (4) was suitable for its intended use in the production of non-sterile drug products.

Misbranded Drug Products

The ineligible drug products you compounded are intended for conditions 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.[3] Accordingly, these ineligible drug products are misbranded under section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)]. Further, it is also 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 misbranded.

D. Corrective Actions

We have reviewed your firm's responses, dated June 26, 2017, and January 10, 2018, as well as your subsequent correspondence. While it appears that your firm has addressed the observations noted on the Form FDA 483, we have the following concerns:

1. According to your response dated January 31, 2018, you are "currently evaluating the appropriateness of the new tripod to determine whether to move it outside of the ISO 5 environment." The tripod holds a cell phone that is used to take pictures for documentation purposes within the ISO 5 area. However, any equipment introduced into the ISO 5 should be easily cleanable and appropriate for cleanroom use.

2. Your firm received a "maximum count for Class 5 exceeded" inside your new ISO 5 hood prior to resuming sterile production. Your corrective action involved re-cleaning the ISO 5 hood, including the dust noted, by removing the filter grate covering the HEPA filter. Subsequently you performed viable air sampling and resumed non-hazardous sterile production after receiving "no growth" results. However, it does not appear that your firm assessed the potential impact of removing and re-installing the filter grate on the integrity of the HEPA filter, please provide documentation that the ISO 5 hood is operating adequately.

3. Your firm has confirmed purchasing and using (b) (4) for non-sterile drug production. However, no additional information was provided for our review, including the date of receipt, start date of use, and the certificate of analysis of the (b) (4) (b) (4).

As explained above, drug products compounded using (b) (4) are not eligible for the exemptions provided by section 503A of the FDCA because (b) (4) is not the subject of an

[3] Your ineligible drug products are not exempted from the requirements of section 502(f)(1) of the FDCA by regulations issued by the FDA (see, e.g., 21 CFR 201.115).

applicable USP or NF monographs, is not a component of FDA-approved human drugs, and does not appear on the 503A bulks list.[4]

We note your June 26, 2017, response stating that your firm removed (b) (4) from your inventory and from the pharmacy's electronic re-order list. We remind you that should you compound and distribute drug products that do not meet the conditions of section 503A, the compounding and distribution of such drugs would be subject to the new drug approval requirement, the requirement to label drug products with adequate directions for use, and the drug CGMP regulations.

E. 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.

Within thirty (30) working days of receipt of this letter, please notify this office in writing if you have taken any steps to correct the remaining concerns. 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 the corrective actions within thirty (30) working days, state the reason for the delay and the time within which you will complete the correction.

Please reference unique identifier CMS 564739 on all correspondence and send to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
19701 Fairchild Road
Irvine, CA 92612

If you have questions regarding this letter, please contact Mr. William V. Millar, Compliance Officer, at (510) 337-6896, or by email at william.millar@fda.hhs.gov.

Sincerely,

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV

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FEI 301354438

[4] See footnote 2 above.