U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations I
10 Waterview Blvd, 3rd FL
Parsippany, NJ 07054
Telephone: (973) 331-4900
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www.fda.gov

CMS # 564363

September 25, 2018

VIA UPS OVERNIGHT
Pramod K. Sharma
Vice President, Quality
ImprimisRx NJ, LLC
1705 Route 46, Suite 6A
Ledgewood, NJ 07852-9720

Dear Dr. Sharma:

From May 30, 2017 to July 10, 2017, a U.S. Food and Drug Administration (FDA) investigator inspected your facility, ImprimisRx NJ, LLC, located at 1705 Route 46 Suite 6A, Ledgewood, NJ 07852. During the inspection, the investigator 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.

Based on this inspection, it appears your firm produced drugs that violate the FDCA.

A. Compounded Drug Products Under the FDCA

Section 503A 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.

[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 FDCA.

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 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

Drug products produced by your firm failed to meet the conditions of section 503A. For example, your firm compounded drug products using artesunate. Drug products compounded using artesunate 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 monograph, is not a component of an FDA-approved human drug and does not appear on the 503A bulks list.[2]

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

Specific violations are described below.

C. Violations of the FDCA

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

[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. Artesunate is not the subject of an applicable USP or NF monograph or a component of an FDA-approved drug and was not nominated for inclusion on the 503A bulks list. 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.

[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).

products are misbranded under section 502(f)(1) 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.

Adulterated Drug Products

The FDA investigator noted 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. Specifically, the investigator observed that your firm failed to perform adequate smoke studies under dynamic conditions to demonstrate unidirectional airflow within the ISO 5 area. Therefore, your products intended to be sterile are produced in an environment that may not provide adequate protection against the risk of contamination.

Moreover, the ineligible drug products compounded in your facility were adulterated due to CGMP violations. *See* section 501(a)(2)(B) of the FDCA. The violations include, for example, your firm's failure 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 (21 CFR 211.113(b)).

D. Corrective Actions

We have reviewed your facility's response. Your corrective action regarding inadequate smoke studies appears adequate.

However, as noted above, drug products compounded using artesunate are not eligible for the exemptions provided by section 503A of the FDCA because artesunate is not the subject of an applicable USP or NF monograph, is not a component of an FDA-approved human drug and does not appear on the 503A bulks list. [4] Should you continue to 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 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 the corrective actions within 30 working days, state the reason for the delay and the time within which you will complete the correction.

[4] See footnote 2 above.

Your written response should refer to the reference number above and be sent to:

Barbara Wilimczyk-Macri, Compliance Officer
U.S. Food and Drug Administration
10 Waterview Blvd 3rd Floor
Parsippany, NJ 07054.
Email: orapharm1_responses@fda.hhs.gov

If you have questions regarding the contents of this letter, please contact Ms. Wilimczyk-Macri by phone at (973) 331-4951 or email at barbara.wilimczyk@fda.hhs.gov.

Sincerely,

Craig W. Swanson -S

Digitally signed by Craig W. Swanson -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300092363, cn=Craig W. Swanson -S
Date: 2018.09.25 11:48:49 -04'00'

For Diana Amador-Toro
Program Division Director/District Director
Division of Pharmaceutical Quality Operations I
New Jersey District Office