# Fagron Compounding Services LLC dba Fagron Sterile Services 11/28/17

Division of Pharmaceutical
Quality Operations III
300 River Place, Suite 5900
Detroit, MI 48207
Telephone: (313) 393-8100
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November 28, 2017

**WARNING LETTER**

**Case# 537637**

**UPS NEXT DAY**
**SIGNATURE REQUIRED**

Gregory A. Rockers, R.Ph., President
Fagron Compounding Services, LLC
dba Fagron Sterile Services
8710 E. 34th St. North
Wichita, KS 67226-2636

Dear Mr. Rockers:

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 October 2, 2015, and again on October 27, 2016. From August 29, 2016, to September 21, 2016, an FDA investigator inspected your facility, Fagron Compounding Services, LLC dba Fagron Sterile Services, located at 8710 E. 34th St. N., Wichita, KS 67226. During the inspection, the investigator 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 September 21, 2016. FDA acknowledges receipt of your facility's response, dated October 7, 2016. Based on this inspection, it appears you produced drugs that violate the FDCA.

**A. Compounded Drug Products under 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.[2]

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**

The FDA investigator 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 adequate written responsibilities and procedures applicable to the quality control unit (21 CFR 211.22(d)).

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. (21 CFR 211.192).

3. Your firm does not have, for each batch of drug product, appropriate laboratory determination of satisfactory conformance to final specifications for the drug product, including the identity and strength of each active ingredient, prior to release (21 CFR 211.165(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.

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, dated October 7, 2016.

Your response regarding your failure to review all deviations and their effects on the quality of finished products was not adequate. You stated in your response that you did not review records of your building management system’s (BMS) alarms concurrently with your production batch records prior to release because most of the BMS’ 766 alarms were not actually critical. You did not explain, however, why most alarms were considered “critical” at the time of the inspection, nor did you provide a rationale for which alarms you do consider critical and which you do not consider critical. Additionally, you committed to update your BMS procedure, but did not provide the updated procedure.

We are unable to fully evaluate the following corrective actions due to lack of adequate supporting documentation.

1. Your firm did not adequately train and qualify operators who perform visual inspection of syringes filled with finished drug products. In addition, the operators did not follow your SOP for visual inspection. In your response, you stated that you revised your SOP “visual inspection and defect recognition” accordingly. However, you did not provide the revised SOP as supporting documentation.

2. Your firm released a batch of finished drug product without conducting post-use filter integrity testing. You stated in your response that you released mitomycin lot 160406@001F after reviewing all the release test results and environmental monitoring results. However, releasing products solely based on product release test results and environmental monitoring test results is not adequate. You committed to implement your Product Release SOP to include log sheet of critical equipment, but this revised SOP was not provided for our evaluation.

In addition to the issues discussed above, you should note that CGMP includes the implementation of oversight and controls over the manufacture of drugs to ensure quality, including managing the risk of and establishing the safety of raw materials, materials used in drug manufacturing, and finished drug products. *See* section 501 of the FD&C Act, as amended by the Food and Drug Administration Safety and Innovation Act (Public Law 112-144, Title VII, section 711). 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.

**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.

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 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 you cannot complete corrective action within 15 working days, state the reason for the delay and the time within which you will complete the correction.

Please address your reply via email to: ORAPharm3_Responses@fda.hhs.gov

Eric Mueller, Compliance Officer
U.S. Food and Drug Administration
Division of Pharmaceutical Quality Operations Division III

Your written notification should refer to the Warning Letter Number above (Case# 537637). If you have questions regarding the contents of this letter, please contact Eric Mueller at (402) 331-8536 ext. 101.

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

cc:
Hans Stoles
Chief Executive Officer
Fagron Group, B.V.
3062 ME Rotterdam
Rotterdam, NL

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

[2] 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 503B of the FDCA.