Infusion Options, Inc. 3/21/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
New York District
158-15 Liberty Ave.
Jamaica, NY 11433-1034

Telephone: 718-340-7000
Facsimile: 718-662-5661

March 21, 2016

WARNING LETTER NYK-2016-29

UNITED PARCEL SERVICE
DELIVERY SIGNATURE REQUESTED

Ms. Estee Altman, R.Ph., Chief Executive Officer/Director
Mr. Robert Naldi, President
Infusion Options, Inc.
5924 13th Avenue
Brooklyn, NY 11219-4934

Dear Ms. Altman and Mr. Naldi:

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 January 24, 2014, and again on December 23, 2014. From April 9 to April 23, 2014, FDA investigators inspected your facility, Infusion Options, Inc., located at 5924 13th Avenue Brooklyn, NY 11219-4934. 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 environmental monitoring for viable air in the ISO 5 zone is not performed. In addition, your firm does not have a routine program for daily monitoring of operators' gloves. Furthermore, your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 area in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk. 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 Form FDA 483 to your facility on April 23, 2014. FDA acknowledges receipt of your facility's response, dated May 14, 2014.

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

The investigators noted that drug products that were intended or expected to be sterile were prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth or rendered injurious to health, causing them to be adulterated within the meaning of section 501(a)(2)(A) of the FDCA. Furthermore, 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, FDA investigators noted:

1. Some of your facility's drug products do not include the following information on the product labels: the dosage form, phone number and address of your facility, and the statements "Office Use Only," "Not for Resale," and "This is a compounded drug."

2. In addition, some of your products do not include the route of administration on the container, and one of your products does not list the inactive ingredients on the drug product label nor on the container and does not include information 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)]].
3. Your facility failed to submit a report to FDA in June 2014 identifying all of the drug products that you compounded during the previous 6-month reporting 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 of the FDCA, 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]

Specific violations are described below.

Adulterated Drug Products

FDA investigators noted that drug products compounded in your facility that were 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 observed that environmental monitoring for viable air in the ISO 5 zone is not performed. In addition, your firmdoes not have a routine program for daily monitoring of operators' gloves. Furthermore, your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 area in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

FDA investigators also 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 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)).

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 failed to ensure that manufacturing personnel wear clothing appropriate to protect drug product from contamination (21 CFR 211.28(a)).

4. Your firm failed to 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.

Failure to Report Drugs

As noted above, your facility failed to submit a report to FDA in June 2014 identifying all of the drug products that you compounded during the previous six-month reporting period. (Section 503B(b)(2) of the FDCA [21 U.S.C. §353b(b)(2)]). Outsourcing facilities are required to submit a report "identifying the drugs compounded by such outsourcing facility during the previous 6-month period." 503B(b)(2)(A)(i). This drug product reporting requirement applies to all drug products compounded by an outsourcing facility; it does not matter whether they are compounded pursuant to a patient-specific prescription or not. 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)].

Misbranded Drug Products

You compounded drug products that are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, and adequate directions cannot be written for them 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). 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.

C. Corrective Actions

In your May 14, 2014, response letter you described certain corrective actions you are planning to take in response to the Form FDA 483 inspectional observations. Although some of your proposed corrective actions appear adequate, others are deficient. For example, your proposed frequencies for environmental monitoring and personnel monitoring are inadequate. In addition, your certification report for air flow studies (smoke studies) did not include the specific dynamic conditions under which the studies and tests were conducted. Finally, your media fill studies do not closely

simulate your aseptic manufacturing operations incorporating, as appropriate, worst-case activities and challenging conditions.

In your May 14, 2014 response letter, you indicate that your firm operates as both a "section 503A pharmacy" and an outsourcing facility. You state that you "respectfully offer a different position from the FDA's measurement of [your firm's] practice against drug manufacturing cGMPs requirements" and that you are subject to and follow the United States Pharmacopeia (USP) Good Compounding Practices. As stated above, outsourcing facilities must comply with CGMP requirements under section 501(a)(2)(B) of the FDCA.[3]

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 (NYK-2016-29). Please address your reply to CDR Frank Verni, Compliance Officer, at the address above.

If you have questions regarding the contents of this letter, please contact CDR Frank Verni at (718) 662-5702.

Sincerely,
/S/
Ronald M. Pace

District Director
New York District

cc:

New York State Education Department
Office of the Professions
State Board of Pharmacy
Attn: Lawrence H. Mokhiber, Executive Secretary
89 Washington Avenue
Albany, New York 12234-1000

New York State Department of Health
Attn: Dr. Howard A. Zucker, Acting Commissioner (redacted copy)
Corning Tower
Empire State Plaza,
Albany, NY 12237

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[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)].

[3] One of the conditions that must be met in order for a drug product to qualify for the exemptions provided in section 503B is that "[T]he drug is compounded in an outsourcing facility in which the compounding of drugs occurs only in accordance with [section 503B]." [Section 503B(a)(11) of the FDCA [21 U.S.C. §353b(a)(11)]]. FDA has also issued a guidance, *For Entities Considering Whether to Register As Outsourcing Facilities Under Section 503B of the Federal Food, Drug, and Cosmetic Act.* This guidance states as follows, "[i]f you register a facility as an outsourcing facility, you are indicating your intent for the facility's compounded drugs to be regulated under section 503B of the FD&C Act. Under section 503B(a)(11), a compounded drug can only qualify for the exemptions from sections 502(f)(1), 505, and 582 of the FD&C Act only if ***all*** of the facility 's compounded drugs are compounded in accordance with section 503B." This guidance provides potential outsourcing facility registrants additional information about the regulatory impact of registering as an outsourcing facility.