Innovative Intrathecal Solutions, Inc. dba Innovative Compounding Pharmacy 9/19/18

WARNING LETTER

VIA SIGNATURE CONFIRMED DELIVERY

September 19, 2018

Nasim P. Barrack
Pharmacist-in-Charge
Innovative Intrathecal Solutions, Inc.
dba Innovative Compounding
41538 Eastman Dr., Suite A
Murrieta, CA 92562

Dear Mr. Barrack:

From October 2, 2017, to December 18, 2017, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Innovative Intrathecal Solutions, Inc., dba Innovative Compounding Pharmacy, located at 41538 Eastman Dr., Suite A, Murrieta, CA 92562. 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. The investigators also noted serious deficiencies in your practices for producing sterile drug products, which put patients at risk.

FDA issued a Form FDA 483 to your firm on December 18, 2017. FDA acknowledges receipt of your facility's response, dated December 26, 2017. Based on this inspection, it appears that you produced drug products 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.

B. Failure to Meet the Conditions of Section 503A

During the inspection, the FDA investigators noted that drug products produced by your firm failed to meet the conditions of section 503A. Specifically, the investigators noted your firm

did not receive valid prescriptions for individually-identified patients for a portion of the drug products you produced.

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

Adulterated Drug Products

The FDA investigators 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. For example, the investigators observed:

1. Your operator using a non-sterile wipe to clean the interior surfaces on an ISO-5 work area, and the rubber stopper of a product vial, during the production of a sterile drug product.

2. Your ISO 7 classified cleanroom contains difficult to clean items such as a hand-held calculator, computer keyboard, and many pieces of paper, which are particle generating.

3. Your firm failed to conduct filter integrity testing following sterile filtration of drug products. Rather, you rely on a subjective assessment by the operator to evaluate the integrity of the filter during the filtration process.

Furthermore, the manufacture of the ineligible drug products is subject to FDA's CGMP regulations, Title 21, Code of Federal Regulations (CFR), parts 210 and 211. The FDA investigator observed significant CGMP violations at your facility, causing the ineligible drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA. The violations included, for example:

1. Your firm failed to establish an adequate system for cleaning and disinfecting the room and equipment to produce aseptic conditions (21 CFR 211.42(c)(10)(v)).

2. Your firm failed to maintain the buildings used in the manufacture, processing, packing, or holding of a drug product in a clean and sanitary condition (21 CFR 211.56(a)).

3. 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)).

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

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

6. Your firm failed to establish and follow an adequate written testing program designed to assess the stability characteristics of drug products and to use results of such stability testing to determine appropriate storage conditions and expiration dates (21 CFR 211.166(a)).

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

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.

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.[2] Accordingly, these ineligible drug 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.

D. Corrective Actions

We have reviewed your firm's responses. We acknowledge that on December 7, 2017, you stated that your firm will comply with section 503A of the Federal Food, Drug and Cosmetic Act and "will cease to provide office stock effective immediately 12/7/2017." Regarding the insanitary conditions, we cannot fully evaluate the adequacy of the following corrective actions described in your December 26, 2017 response because you did not include sufficient information or supporting documentation:

1. You state that you now require the use of sterile wipes for cleaning the ISO 5 areas; however, you did not include sufficient information or supporting documentation (e.g., sterile wipes labeling, updated cleaning procedure(s), etc.).

2. Regarding the failure to conduct filter integrity testing, you state that you purchased the appropriate equipment, and that it is in place and being used; however, you did not include sufficient information or supporting documentation (e.g., bubble point tester invoice and/or labeling, updated procedure(s), etc.).

Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether drug products you compound meet the conditions of section

503A, including the condition on receipt of a prescription for an identified individual patient prior to compounding and distributing drug products.

Should your facility 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 requirements. Before doing so, you must comply with the requirements of section 505 and 502(f)(1) and fully implement corrections that meet the minimum requirements of the CGMP regulations.[3]

In addition to the issues discussed above, you should note that CGMP requires the implementation of quality oversight and controls over the manufacture of drugs, including the safety of raw materials, materials used in drug manufacturing, and finished drug products. *See* section 501 of the FDCA. 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 first undertake a comprehensive assessment of operations, including facility design, procedures, personnel, processes, maintenance, materials, and systems. This review should assess your aseptic processing operations. A third-party consultant with relevant sterile drug processing 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.

In addition, based on our review of photographic evidence obtained by the FDA investigators during the inspection of your facility, the Agency is concerned with the suitability of the work surfaces within your ISO 5 production areas. The work surfaces appear to be constructed of a laminate material, which may be porous, difficult to clean and be a reservoir for microbial contamination. In addition, your cleanroom was noted to contain other items, such as cabinets, which also appear to be constructed of a laminate material. In your response,

describe the materials used to construct these items and provide supporting documentation to demonstrate that all of these items are suitable for use in your ISO classified areas.

Please address your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
United States Food and Drug Administration
19701 Fairchild
Irvine, California 92612

If you have any questions about the content of this letter, please contact Jessica Mu, Compliance Officer, at 949-608-4477 and reference unique identifier CMS 555295 on all correspondence.

Sincerely,
/S/
CDR Steven E. Porter, Jr.
Program Division Director
Division of Pharmaceutical Quality Operations IV

Cc: Virginia Herold, Executive Officer (Via E-mail)
California State Board of Pharmacy
1625 N. Market Boulevard, Suite N-219
Sacramento, CA 95834

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[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.

[2] 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).

[3] In this letter, we do not address whether your proposed corrective actions would resolve the CGMP violations noted above.