Oregon Compounding Centers, Inc. dba Creative Compounds 1/27/15

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Seattle District
Pacific Region
22215 26th Ave SE, Suite 210
Bothell, WA 98021

Telephone: 425-302-0340
FAX: 425-302-0402

January 27, 2015

OVERNIGHT DELIVERY
SIGNATURE REQUIRED

In reply refer to Warning Letter SEA 15-08

Denise S. Burnham, President
Oregon Compounding Centers, Inc.
dba Creative Compounds
8560 SW Salish Lane
Suite 100
Wilsonville, Oregon 97070-9625

WARNING LETTER

Dear Ms. Burnham:

From August 4, 2014, to August 28, 2014, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility located at 8560 SW Salish Lane, Suite 100, Wilsonville, Oregon. During the inspection, the investigators noted that you were not receiving valid prescriptions for individually-identified patients for a portion of the drug products you were producing. The investigators also noted that your firm makes domperidone drug products. Domperidone is not the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, nor is it a component of an FDA-approved human drug product, and it does not appear on a list developed by the Secretary under section 503A(b)(1)(A)(i)(III) of the Federal Food, Drug, and Cosmetic Act (FDCA) [21 U.S.C. § 353a (b)(1)(A)(i)(III)]. In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at

risk. For example, they observed that equipment and materials are not disinfected before introduction into the ISO 5 area. The investigators also observed operators processing sterile drug products with exposed skin on their wrists. Furthermore, investigators found that 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 issued a Form FDA-483 to your facility on August 28, 2014, and subsequently issued an amended Form FDA-483 on September 12, 2014.

Based on this inspection, it appears that you are producing drugs that violate the FDCA.

A. Compounded Drugs Under the FDCA

Section 503A of the FDCA [21 U.S.C. § 353a] describes the conditions under which certain compounded human drug products are entitled to exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) (section 501(a)(2)(B) of the FDCA [21 U.S.C. § 351(a)(2)(B)]); labeling with adequate directions for use (section 502(f)(1) of the FDCA [21 U.S.C. § 352(f)(1)]); and FDA approval prior to marketing (section 505 of the FDCA [21 U.S.C. § 355]). Receipt of valid prescriptions for individually-identified patients is one of the conditions necessary to qualify for the exemptions under section 503A of the FDCA. During the FDA inspection, the investigators observed that your firm does not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce, and that you produce domperidone.

In addition, compounded drug products containing domperidone are not eligible for the exemptions under section 503A of the FDCA because domperidone is not the subject of an applicable USP or NF monograph, is not a component of an FDA-approved human drug, and it does not appear on a list of bulk drug substances that may be used for compounding developed by the Secretary.

Accordingly, the drugs you compound without valid prescriptions for individually-identified patients and any drug products you compound using domperidone, which is not the subject of an applicable USP or NF monograph, not a component of an FDA-approved human drug product, and does not appear on a list developed by the Secretary under section 503A(b)(1)(A)(i)(III),are not entitled to the exemptions in section 503A.

In addition, we remind you that there are other conditions that must be satisfied to qualify for the exemptions in section 503A of the FDCA.**[1]**

B. Violations of the FDCA

The domperidone drug products that your firm manufactures and distributes and the drug products that your firm manufactures and distributes without valid prescriptions for individually-identified patients are misbranded drugs in violation of section 502(f)(1) of the FDCA. In addition, your sterile drug products are prepared, packed, or held under insanitary conditions whereby they may have been contaminated with filth, or whereby they may have been rendered injurious to health. As such, all sterile products you manufacture are adulterated within the meaning of section 501(a)(2)(A) of the FDCA [21 U.S.C. § 351(a)(2)(A)]. Furthermore, because you manufacture and distribute a portion of your drugs without valid prescriptions for individually-identified patients, and also domperidone drug products (which, as noted above, are not eligible for the exemptions provided by section 503A(a)), the manufacture of these drugs is also subject to FDA's Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (CFR), Parts 210 and 211. FDA investigators observed significant CGMP violations at your facility, causing such drug products to be adulterated within the meaning of section 501(a)(2)(B) of the FDCA.

Misbranded Drug Products

Because the domperidone drug products and the drug products for which you have not obtained valid prescriptions for individually-identified patients are intended for conditions that are not amenable to self-diagnosis and treatment by individuals who are not medical practitioners, 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 [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.

Adulterated Drug Products

Additionally, FDA investigators observed that your sterile drug products 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, investigators observed that equipment and materials are not disinfected before introduction into the ISO 5 area. The investigators also observed operators processing sterile drug products with exposed skin on their wrists. Furthermore, investigators found that 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.

The FDA investigators also observed CGMP violations at your facility, causing the drug products for which you have not obtained valid prescriptions for individually-identified patients to be adulterated under section 501(a)(2)(B) of the FDCA. The violations include, 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 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)).

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

5. 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)).

6. 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).

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 adulterated.

C. Corrective Actions

FDA acknowledges your voluntary recall of all aseptically filled sterile drug products produced between July 1, 2014, and September 22, 2014, that were within expiry, and your action to cease compounding all sterile products on October 3, 2014. We also acknowledge receipt of your response to the Form FDA 483 dated October 30, 2014, in which you state that your firm is "no longer dispensing any non-patient specific compounded products for Office Use or any other reason," and that you have hired consultants to assist with implementing corrective actions. We also acknowledge your responses dated October 1, October 6, October 9, October 30, 2014, and December 9, 2014.

In your responses, you described certain corrective actions you took in response to the Form FDA-483 observations. Your firm's planned corrections will be verified during FDA's next inspection.

Please be aware that section 501(a)(2)(A) of the FDCA concerning insanitary conditions applies regardless of whether the drugs are compounded and distributed after receipt of a prescription for an identified individual patient. In addition, should you manufacture and distribute domperidone drug products or drug products without valid prescriptions for individually-identified patients, the manufacture of such drugs would be subject to FDA's drug CGMP regulations (21 CFR Parts 210 and 211), among other requirements described above, and, before doing so, you should fully implement corrections that meet the minimum requirements of 21 CFR Part 211 in order to provide assurance that the drug product(s) produced by your firm conform to the basic quality standards that ensure safety, identity, strength, quality, and purity.

FDA strongly recommends 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.

In addition, you should correct the violations of FDCA section 502(f)(1) noted above.

D. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of the 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 assure that your firm complies with all requirements of federal law and 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 may re-inspect to ensure that your firm complies with all requirements of federal law and FDA regulations.

Within fifteen 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 actions within 15 working days, state the reason for the delay and the time within which you will complete the correction. In addition to taking appropriate corrective actions, you should notify this office prior to resuming production of any sterile drugs in the future. Your written notification should be addressed to:

Jessica L. Kocian
Compliance Officer
U.S. Food and Drug Administration
22215 26th Avenue SE, Suite 210
Bothell, WA 98021

Refer to the Unique Identification Number (SEA 15-08) when replying. If you have questions regarding any issues in this letter, please contact Ms. Kocian at 425-302-0444.

Sincerely,
/S/
Miriam R. Burbach
District Director

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[1] For example, section 503A also addresses anticipatory compounding, which includes compounding (not distribution) before receipt of a valid prescription order for an individual patient. We are not addressing anticipatory compounding here