Pacific Healthcare, Inc dba B&B Pharmacy 9/2/16

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Los Angeles District
Pacific Region
19701 Fairchild
Irvine, CA 92612-2506
Telephone: 949-608-2900
FAX: 949-608-4415

WARNING LETTER

VIA UNITED PARCEL SERVICE
SIGNATURE REQUIRED

September 2, 2016

WL# 45-16

Hyun Joon (Eugene) Ro, Pharm.D.
Pacific Healthcare, Inc., dba B&B Pharmacy
10244 Rosecrans Avenue
Bellflower, CA 90706

Dear Dr. Ro:

Between August 3, 2015, and August 18, 2015, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Pacific Healthcare, Inc., dba B&B Pharmacy, located at 10244 Rosecrans Avenue, Bellflower, CA 90706.

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. In addition, the investigators observed serious deficiencies in your practices for producing sterile drug products, which put patients at risk. For example, our investigators observed a hood located on top of a laminated wood table, which may harbor contamination. In addition, our investigators observed poor aseptic practices, including an operator disinfecting his gloves with non-sterile isopropyl alcohol (IPA) while performing aseptic operations as well as an operator entering his head with exposed skin into the ISO 5 work zone. The investigators noted that your firm did not use a sporicidal agent, and used non-sterile disinfectants and wipes as part of your disinfection program for the aseptic processing area. Further, the investigators noted that your firm also failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 areas in which sterile products are processed. Therefore, your products may be produced in an environment that poses a significant contamination risk.

Furthermore, FDA investigators collected environmental samples of multiple locations in your facility, including the aseptic processing areas. Testing results of the samples identified microbial contamination in the aseptic processing areas, including spore-forming bacteria. We notified you of the results of the samples on September 29, 2015 and October 5, 2015.

FDA issued a Form FDA 483 to your firm on August 18, 2015. FDA acknowledges receipt of your firm's September 3, 2015, response to the Form FDA 483. FDA also acknowledges your action taken on September 23, 2015, to voluntarily recall all sterile drug products within expiry.

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 may qualify for exemptions from three sections of the FDCA: compliance with current good manufacturing practice (CGMP) requirements, 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 for the exemptions under section 503A.

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. Accordingly, the drugs you compound without valid prescriptions for individually-identified patients are not entitled to the exemptions in section 503A of the FDCA.

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

B. Violations of the FDCA

Because the drug products that you manufacture and distribute without valid prescriptions for individually-identified patients are not the subject of approved applications, they are unapproved new drugs and misbranded drugs in violation of sections 505(a) and 502(f)(1) of the FDCA, respectively.

In addition, drug products that are 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 [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, the manufacture of those drugs is subject to FDA's CGMP regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (CFR), Parts 210 and 211. The 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.

Unapproved New Drug Products

You do not have any FDA-approved applications on file for the drug products for which you have not obtained valid prescriptions for individually-identified patients.***2*** Under sections 301(d) [21 U.S.C. §§ 331(d)] and 505(a) of the FDCA, a new drug may not be introduced into or delivered for introduction into interstate commerce unless an application approved by FDA under section 505 of the FDCA is in effect for the drug. Your marketing of these products, or

other applicable products, without an approved application violates these provisions of the FDCA.

Misbranded Drug Products

You compound drug products for which you have not obtained valid prescriptions for individually-identified patients that are intended for conditions that are 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, 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).

The introduction or delivery for introduction into interstate commerce of these products therefore violates sections 301(a) of the FDCA [21 U.S.C. § 331(a)]. It is also 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, the FDA investigators observed that drug products 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, FDA investigators noted that:

1. Your facility was not adequately designed for sterile drug production. Specifically, our investigators noted that one of your hoods is located on top of a laminated wood table that may harbor contamination. In addition, a corner of wood was exposed directly in front of one of your hoods where aseptic production occurred. Furthermore, FDA environmental sample results of that exposed wood identified spore-forming bacteria.

2. Your operators were observed conducting poor aseptic practices. Specifically, an operator was observed disinfecting his gloves with a non-labeled bottle filled with non-sterile IPA during the production of an injectable drug product. In addition, an operator was observed to enter his head into the vertical hood to clean the interior of the hood allowing exposure of bare forehead skin, neck, eyes, and eye brows within the ISO 5 work zone.

3. Your firm did not use a sporicidal agent, and used non-sterile disinfectants and wipes as part of your disinfection program for the aseptic processing area. Furthermore, FDA environmental sample results identified spore-forming bacteria at several locations within your aseptic processing area.

4. Your firm failed to demonstrate through appropriate studies that your hoods are able to provide adequate protection of the ISO 5 areas in which sterile products are processed.

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 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)).

2. 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)).

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

4. 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)).

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 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)).

Under Section 301(a) of the FDCA, 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 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 acknowledge your September 3, 2015, response to the Form FDA 483, which stated your decision to cease compounding sterile drug products. We also acknowledge your action taken on October 7, 2015, to voluntarily recall all compounded sterile drug products within expiry.

In your response, you also quoted information from the FDA website and stated that “[t]his language clearly states that 503[A] pharmacies are exempt from [C]GMP application.” As stated above, because investigators observed that your firm does not receive valid prescriptions for individually-identified patients for a portion of the drug products you produce, those drugs do not qualify for the exemptions in section 503A of the FDCA. Therefore, the manufacture of such drugs is subject to FDA’s drug CGMP regulations, 21 CFR parts 210 and 211.

If you decide to resume production of sterile drugs, FDA strongly recommends that your management 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.

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. You should correct all insanitary conditions at your firm before resuming operations.

In addition, if you were to continue to manufacture and distribute 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), and, before doing so, you should fully implement corrections that meet the minimum requirements of 21 CFR Part 211 to provide assurance that the drug products produced by your firm conform to the basic quality standards regarding safety, identity, strength, quality, and purity. As indicated above, such drug products would also be subject to the new drug approval requirements in section 505 and the requirements for adequate directions for use in section 502(f)(1), among other requirements of the FDCA.

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.

If you decide to resume sterile operations, 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 working days of receipt of this letter, please notify this office in writing if you have taken any specific steps to correct violations, or you may inform us that you do not intend to resume production of sterile drugs. If you intend to resume production of sterile drugs in the future, please include an explanation of the specific steps that you have taken to correct violations. Please include the reference number listed above and 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. In addition to taking appropriate corrective actions, you should notify this office fifteen working days prior to resuming production of any sterile drugs in the future. Your written notification should be addressed to:

Kelly D. Sheppard
Director, Compliance Branch
Food and Drug Administration
Los Angeles District
Pacific Region
19701 Fairchild
Irvine, CA 92612

If you have questions regarding any issues in this letter, please contact Dr. Raymond Brullo via email at Raymond.Brullo@fda.hhs.gov or by phone at 949-608-2918.

Sincerely,
/S/
CDR Steven E. Porter, Jr.
Director, Los Angeles District

cc:

Virginia Herold, Executive Officer
California State Board of Pharmacy
1625 N. Market Boulevard, Suite N-219
Sacramento, CA 95834

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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.

2 The specific products made by your firm are drugs within the meaning of section 201(g) of the FDCA [21 U.S.C. § 321(g)] because they are intended for use in the diagnosis, cure, mitigation, treatment, or prevention of diseases and/or because they are intended to affect the structure or any function of the body. Further, they are “new drugs” within the meaning of section 201(p) of the FDCA [21 U.S.C. §321(p)] because they are not generally recognized as safe and effective for their labeled uses.