Ladd Family Pharmacy LLC 9/26/17

Division of Pharmaceutical
Quality Operations IV
19701 Fairchild, Irvine, CA
92612-2506
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WARNING LETTER

VIA SIGNATURE CONFIRMED DELIVERY

September 26, 2017

Jeremy B. Lundevall, Owner
Ladd Family Pharmacy, LLC
1109 S Broadway Avenue
Boise, Idaho 83706-3626

Dear Mr. Lundevall:

From September 12, 2016, to September 23, 2016, U.S. Food and Drug Administration (FDA) investigators inspected your facility, Ladd Family Pharmacy, LLC, located at 1109 S. Broadway Avenue, Boise, Idaho 83706-3626. 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. In addition, the investigators noted serious deficiencies in your practices for producing drug products, which put patients at risk.

FDA issued a Form FDA 483 to your firm on September 23, 2016. FDA acknowledges receipt of your facility's response, dated October 12, 2016. FDA also acknowledges the notification you distributed to your customers, dated September 22, 2016, which states that "effective *November 1st, 2016* Ladd Family Pharmacy will NO LONGER provide any compounded office use medication that is NOT patient specific." 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 practices (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.

In addition, for a compounded drug product to qualify for the exemptions under section 503A, bulk drug substances used to compound it must: (I) comply with the standards of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph, if a monograph exists, and the USP chapter on pharmacy compounding; (II) if such a monograph does not exist, be components of drugs approved by the Secretary; or (III) if such a monograph does not exist and the drug substance is not a component of a drug approved by the Secretary, appear on a list developed by the Secretary through regulation ("503A bulks list") (section 503A(b)(1)(A)(i) of the FDCA).

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. For example, the investigators collected evidence that indicates:

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

2. Your firm compounded drug products using acidophilus lactobacillus, coenzyme Q10, and melatonin. Drug products compounded using these bulk drug substances are not eligible for the exemptions provided by section 503A(a), because they are not the subjects of applicable USP or NF monographs, are not components of FDA-approved human drugs, and do not appear on the 503A bulks list. [2]

Therefore, you compounded drug products that do not meet the conditions of section 503A and are not eligible for the exemptions 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 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, our investigators observed white powder residue in the joints between the plastic front panel and pivot hinges of **(b)(4)** Hood #**(b)(4)** as well as white powder between the work surface and back panel of **(b)(4)** Hood #**(b)(4)**. This residue was observed on the inside of the hood before and

during manufacturing of drug products. Additionally, our investigators observed a technician using a worn plastic store club card not intended for pharmaceutical or laboratory use, to fill bulk powder drug product into empty gelatin capsules. Furthermore, our investigators noted that the cabinet surrounding the utensil dishwasher was in a state of disrepair due to exposed particle board and posed a risk of contaminating cleaned utensils.

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 investigators 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 clean, maintain, and, as appropriate for the nature of the drug, sanitize and/or sterilize equipment and utensils at appropriate intervals to prevent malfunctions or contamination that would alter the safety, identity, quality, or purity of the drug product beyond the official or other established requirements (21 CFR 211.67(a)).

2. 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)).

3. 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)).

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 any human or animal 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.[3] 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 [21 U.S.C. § 331(k)] to do any act with respect to any human or animal 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 response to the Form FDA 483.

Regarding the insanitary condition observations in the Form FDA 483, some of your corrective actions appear to be adequate; however, others cannot be fully evaluated because your response did not include sufficient information or supporting documentation. For example, in your response to Observation #2 of the Form FDA 483 it is not clear what disinfectants your firm will use to ensure that hazardous drugs, including hormones, are deactivated during cleaning/disinfection.

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 and the condition on compounding drug products using a bulk drug substance that complies with an applicable USP or NF monograph, is a component of an FDA-approved human drug, or appears on the 503A bulks list.

In addition, regarding issues related to the condition of section 503A of the FDCA, your corrective action to discontinue compounding and distributing drugs products for office stock appears adequate. FDA acknowledges your notification to your customers, dated September 22, 2016, which states that "effective *November 1st, 2016* Ladd Family Pharmacy will NO LONGER provide any compounded office use medication that is NOT patient specific."

As explained above, the compounding of drug products using a bulk drug substance that complies with an applicable USP or NF monograph, is a component of an FDA-approved human drug, or appears on the 503A bulks list is a condition of section 503A, which your firm failed to meet for a portion of the drug products you produced. Should you 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 regulations. 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.[4]

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 introduce into interstate commerce 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 for human and animal drugs. In particular, this review should assess your aseptic processing operations. A third party consultant with relevant 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 the violations. Please include an explanation of each step being taken to prevent the recurrence of the 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 fifteen (15) working days, state the reason for the delay and the time within which you will complete the correction.

Your written notification should refer to the Warning Letter Number above (**516046**). Please address your reply to:

CDR Steven E. Porter, Jr.
Director, Division of Pharmaceutical Quality Operations IV
U.S. Food & Drug Administration
19701 Fairchild
Irvine, California 92612

If you have questions regarding any issues in this letter, please contact Ms. Maria P. Kelly-Doggett, Compliance Officer via email at maria.kelly-doggett@fda.hhs.gov or by phone at (425) 302-0427 and reference unique identifier **516046**.

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

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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] On June 9, 2016, FDA issued a final guidance titled, *Interim Policy on Compounding Using Bulk Drug Substances Under Section 503A of the Federal Food, Drug, and Cosmetic Act*. This guidance describes FDA's interim regulatory policy for State-licensed pharmacies, Federal facilities, and licensed physicians that compound human drug products using bulk drug substances that do not otherwise meet the conditions of section 503A(b)(1)(A)(i) while the 503A bulks list is being developed. Specifically, the guidance sets out the conditions under which FDA does not intend to take

action against a State-licensed pharmacy, Federal facility, or licensed physician for compounding a drug product using a bulk drug substance that is not the subject of an applicable USP or NF monograph or a component of an FDA-approved drug, until the substance is identified in a final rule as included or not included on the 503A bulks list. These conditions include that the substance may be eligible for inclusion on the 503A bulks list, was nominated with adequate support for FDA to evaluate it, and has not been identified by FDA as a substance that appears to present significant safety risks pending further evaluation. Acidophilus lactobacillus, coenzyme Q10, and melatonin were nominated for inclusion on the 503A bulks list. They have each been identified as a substance that was not nominated with adequate support for FDA to evaluate the substance. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf.

[3] 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).

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