Reliable Rexall-A Compounding Pharmacy 3/9/17

San Francisco District
1431 Harbor Bay Parkway
Alameda, CA 94502-7070

March 9, 2017

CMS 511750

WARNING LETTER

Via UPS – Signature Required

Sam C.H. Ching, R.Ph.
Attn: Natalia Mazina, Attorney
Kelly, Hockel & Klein, P.C.
44 Montgomery Street, Suite 1500
San Francisco, CA 94104

Dear Mr. Ching:

From March 18, 2016, to March 29, 2016, U.S. Food and Drug Administration (FDA) investigators conducted an inspection of your facility, Reliable Rexall –A Compounding Pharmacy, located at 801 Irving St. San Francisco, CA 94122-2310. This inspection was conducted after receipt of a MedWatch report dated March 2, 2016, associated with a product made by your firm. 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 FDA investigators noted serious deficiencies in your practices for producing non-sterile drug products, which put patients at risk.

FDA issued Form FDA 483s to your firm on March 29, 2016, and April 20, 2016. FDA acknowledges receipt of your facility's responses, dated April 13, 2016. FDA acknowledges your action on March 25, 2016, to voluntarily recall all unexpired lots of compounded drug products. In addition, we acknowledge that you ceased all drug production activities. Further,

FDA acknowledges the June 21, 2016, California Board of Pharmacy (CABOP) order for the surrender of your firm's pharmacy permit and your pharmacist license. The surrender of the pharmacy permit was stayed until July 1, 2016, to allow the sale of the pharmacy.

Based on the inspection, it appears that you produced drug products that violate the FDCA.

A. Compounded Drugs 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 of the FDCA (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).

Another condition for the exemptions under section 503A of the FDCA is that the licensed pharmacist or licensed physician preparing it does not compound a drug product that appears on a list published by FDA at Title 21 CFR Part 216 of drugs that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective ("withdrawn and removed list") (section 503A(b)(C)).

B. Failure to Meet the Conditions of Section 503A

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

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 domperidone. Drug products compounded using domperidone are not eligible for the exemptions provided by section 503A(a), because dompoeridone is not the subject of an applicable USP or NF monograph, is not a component of an FDA-approved human drug, and does not appear on the 503A bulks list.[2]

3. Your firm compounded a drug product containing chloroform (thymol 2%/chloropform 2% liquid), which appears on the withdrawn or removed list at 21 CFR §216.24.[3]

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”.

C. Violations of the FDCA

Adulterated Drug Products

As noted, FDA received a MedWatch report dated March 2, 2016, regarding an adverse event experienced by a patient associated with biotin 100 mg capsules produced by your firm. FDA collected multiple samples of this product for analysis and found that they contained either less than the labeled concentration of biotin (48.4%) or no biotin. In addition, one of the samples labeled as biotin 100 mg, contained 4-aminopyridine instead of biotin. Under section 501(b) of the FDCA [21 U.S.C. § 351(b)], a drug is adulterated if it purports to be or is represented as a drug the name of which is recognized in an official compendium, and its strength differs from, or its quality or purity falls below, the standards set forth in such compendium. The strength of your biotin differed and was below the labeled amount of biotin the product was purported to possess, causing it to be adulterated under section 501(b) of the FDCA.

The manufacture of the ineligible drug products are 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 follow written procedures for production and process control designed to assure that the drug products you manufacture have the identity, strength, quality, and purity they purport or are represented to possess (21 CFR 211.100(b)).

2. Your firm failed to reject any lot of components that did not meet the appropriate written specifications for identity, strength, quality and purity (21 CFR 211.84(e)).

3. 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)).

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.

Unapproved New Drug Products

You do not have any FDA-approved applications on file for the ineligible drug products that you compounded.[4] Under sections 505(a) and 301(d) of the FDCA [21 U.S.C. § 331(d)], 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. Marketing of these products, or other applicable products, without an approved application violates these provisions of the FDCA.

Misbranded Drug Products

Under section 502(a) of the FDCA [21 U.S.C. § 352(a)], a drug product is misbranded if its labeling is false or misleading in any particular. As noted, FDA analyses showed that your products labeled as biotin 100 mg contained less than the labeled concentration of biotin, no biotin, or 4-aminopyridine instead of biotin. Because the labeling of these drug products were false, they were misbranded under section 502(a) of the FDCA.

Additionally, 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, and they are not exempt from the requirements of section 502(f)(1) of the FDCA (*see*, *e.g.*, 21 CFR 201.115). Accordingly, these ineligible drug products are misbranded under section 502(f)(1) of the FDCA. The introduction or delivery for introduction into interstate commerce of these products therefore violates section 301(a) of the FDCA. It is also 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 reviewed your firm's responses to the Form FDA 483 observations. We acknowledge your recall of all unexpired lots of compounded drug products due to concerns of mislabeling. In addition, we acknowledge that you ceased production of all non-sterile drug products due to a concern of lack of quality assurance. Further, we acknowledge that following the CABOP's order directing your firm to surrender its pharmacy permit, your firm was sold in July 5, 2016, and is registered under the new ownership as Reliable Rexall Sunset Pharmacy.

Should you resume compouding and distributing 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.

D. Conclusion

The violations cited in this letter are not intended to be an all-inclusive statement of violations at your facility. Please confirm whether you still own this firm or if it is under new ownership. The owner of the pharmacy is 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 the owner's responsibility to ensure that the firm complies with all requirements of federal law and FDA regulations.

The owner 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 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.

Your written notification should reference the unique identifier **511750**. Please addressed your reply to:

Lawton W. Lum, Director of Compliance Branch
San Francisco District Office
1431 Harbor Bay Parkway
Alameda, CA 94505-7070

If you have questions regarding any issues in this letter, please contact Compliance Officer Lance De Souza via email at lance.desouza@fda.hhs.gov or by phone at (510) 337-6873.

Sincerely,
/S/
Darla R. Bracy
Acting District Director
San Francisco District

cc:
Sean Weeks, Owner
William Steel
Reliable Rexall Sunset Pharmacy
801 Irving St.
San Francisco, CA 94122-2310

Virginia Herold, Executive Officer
California State Board of Pharmacy
1625 N Market Street
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] Domperidone was nominated for inclusion on the list of bulk drug substances that can be used in compounding that must be developed through regulation pursuant to section 503A(b)(1)(A)(i)(III) of the FDCA (503A bulks list). See section 503A(b)(1)(A)(i)(III). 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. Domperidone

has been identified as a substance that appears to present significant safety risks. For additional information, see the guidance at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM469120.pdf.

[3] The withdrawn or removed list includes all drug products containing chloroform.

[4] The specific products made by your firm are drugs within the meaning of section 201(g) of the Act, [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) [21 U.S.C. 321(p)] of the FDCA because they are not generally recognized as safe and effective for their labeled uses.

Response Letter

- Reliable Rexall-A Compounding Pharmacy - Response Letter 3/20/17