Division of Pharmaceutical Quality
Operations Ill
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Detroit, Ml 48207
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June 29, 2017

WARNING LETTER

Case# 515029

UPS NEXT DAY
SIGNATURE REQUIRED

Mr. Ronald D. Whitt
CEO/Owner
ChemRite CoPac, Inc.
19725 W. Edgewood Dr.
Lannon, WI 53046-9738

Dear Mr.Whitt:

The U.S. Food and Drug Administration (FDA) conducted an inspection of your drug manufacturing facility, ChemRite CoPac, Inc., at 19725 W. Edgewood Dr., Lannon, WI, from June 6 to July 15, 2016.

This inspection revealed that your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, therefore making your drug products adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), 21 U.S.C. 351(a)(2)(B).

This warning letter summarizes significant violations of current good manufacturing practice (CGMP) regulations for finished pharmaceuticals. See Title 21, Code of Federal Regulations (21 CFR, Part 210 and 211).

We reviewed your August 4, 2016, response in detail.

During our inspection, our investigators observed specific violations including, but not limited to, the following.

1. Your firm failed to maintain adequate separate defined areas necessary to prevent contamination or mix-up (21 CFR 211.42(c)).

You manufacture several over-the-counter (OTC) oral rinses and oral moisturizing drug products, including **(b)(4)**, **(b)(4)** Mouth Moisturizer, and **(b)(4)** Oral Solution, for your customer, **(b)(4)** Products Inc. You manufacture these oral drug solutions using the same equipment that you use to manufacture numerous non-pharmaceutical materials in your facility, including an industrial car care product, **(b)(4)** Polish and Sealant.

This car care product is paraffin-based and labeled as "Harmful or fatal if swallowed" and "Keep out of reach of children." You also manufacture other toxic non-pharmaceutical industrial and automotive care products, such as leather treatments (**(b)(4)** Leather Care, **(b)(4)** Leather Lotion) and sealants (**(b)(4)** Poly Sealant), using the same mixing tank and filling line you use for OTC oral drug products.

The ingredients in your non-pharmaceutical products are extremely difficult to remove from manufacturing equipment, and could contaminate the drug products that you manufacture on shared equipment, such as the various oral solutions discussed above. It is unacceptable as a matter of CGMP to continue manufacturing drugs using the same equipment that you use to manufacture toxic industrial-grade car care products.

In response to this letter, discontinue manufacturing drugs on shared equipment in your facility. If you intend to continue to manufacture both pharmaceutical and non-pharmaceutical products at your facility, provide a plan to show how you will separate the areas in which you will maintain dedicated manufacturing equipment for your pharmaceutical manufacturing and industrial product manufacturing operations.

In addition, conduct a risk assessment for all drugs you have previously produced on equipment shared with industrial products. For each product, assess the risk of potential contamination due to the shared equipment, and provide your plans for addressing the product quality and patient safety risks for any product still in distribution, including potential recalls or market withdrawals.

2. Your firm does not have, for each batch of drug product, appropriate laboratory testing, as necessary, of each batch of drug product required to be free of objectionable organisms (21 CFR 211.165(b)).

You released at least 24 batches of your OTC drug product **(b)(4)** between 2013 and 2015 without performing analyses to assess whether they met all microbiological finished product specifications. Your batch records for this drug report results for analysis of the objectionable organism *Pseudomonas aeruginosa* of less than 1 colony forming unit/ml. However, the test results provided to you by your contract test laboratory did not report the results of any *P.*

aeruginosa analysis. We also reviewed the raw data for the microbiological tests performed by your contract testing laboratory. We found that there was no raw data to indicate that the contract testing laboratory had performed *P. aeruginosa* analysis. Despite these discrepancies, you released multiple batches of this drug.

In your response, you stated, "A process deviation report was initiated on 8-1-2016. The report cites the favorable microbial results obtained from the customer. The results will demonstrate that the target or observed pathogen was effectively absent from the bulk material upon receipt."

Your response is inadequate. The effective absence of *P. aeruginosa* from materials tested by your customer does not satisfy the requirement that you perform appropriate laboratory testing on your drugs to ensure that the drugs meet their microbiological specifications before you release them for distribution. You failed to conduct retrospective testing on your retain samples for lots of this drug that you released without complete testing for all required specifications. Moreover, you failed to explain why your batch records report the absence of *P. aeruginosa* when the test results you received from your contract testing laboratory do not contain information about this type of testing.

In response to this letter, provide your investigation into your failure to perform the required testing for objectionable organisms. Include your root cause analysis, a timeline for completing retain testing, and a summary of your retrospective review of all released lots of **(b)(4)**. Also evaluate and provide a report on all other lots of drugs you have distributed, within expiry, to determine whether you released any of them without complete or adequate microbiological testing.

3. Your firm failed to establish an adequate quality control unit with the responsibility and authority to approve or reject all components, drug product containers, closures, in-process materials, packaging material, labeling, and drug products, including drug products manufactured, processed, packed or held under contract by another company (21 CFR 211.22(a)).

Your oversight and control over the drugs manufactured for you under contract by other companies, especially your contract testing laboratories, is inadequate. For example, your quality unit failed to recognize that the contract laboratory that performs microbiological testing for you did not appropriately validate its test method for the presence of *Burkholderia cepacia*. Your quality unit approved release of the drugs that your contract laboratory had tested using inadequately validated test methods.

During an inspection of your customer, **(b)(4)**, FDA investigators collected certificates of analysis that listed the absence of *B. cepacia* as one of your specifications for release of **(b)(4)**. However, we found that at the time that we inspected your facility, your contract laboratory had not adequately validated its method for culturing and identifying *B. cepacia* in your firm's finished drug products. Your contract laboratory did not include *B. cepacia* as a challenge organism, according to its December 18, 2013, Microbial Recovery Validation Report. The same contract laboratory was using a draft working procedure while performing the *B. cepacia* analysis. Your quality unit received test results from this contract testing laboratory and relied on

them in releasing your product to your customer, even though the laboratory's test methods were inadequate.

In response to this letter, provide your root cause for your quality unit's failures related to *B. cepacia* testing performed on your behalf by your contract laboratory. Provide an update regarding your contractor qualification, selection, and oversight program to demonstrate how your quality unit determines that each of your contract testing laboratories uses methods that have been validated for their intended use.

Repeat observations at facility
In previous inspections, dated February 7 to 21, 2013, and March 9 to 24, 2016, FDA cited similar CGMP observations. You proposed specific remediation for these observations in your responses. These repeated failures demonstrate that your facility's oversight and control over the manufacture of drugs is inadequate.

Responsibilities as a contractor
Firms acting as contract manufacturers for various aspects of drug manufacturing must comply with CGMP. FDA is aware that many pharmaceutical product manufacturers use independent contractors, such as production facilities, testing laboratories, packagers, and labelers. FDA regards contractors as extensions of the manufacturer.

You are responsible for the quality of drugs you produce, regardless of agreements in place with your customers or the contractors on whom you rely to perform testing for you. You are required to ensure that drugs are made in accordance with section 501(a)(2)(B) of the FD&C Act for safety, identity, strength, quality, and purity.

For guidance on clarifying roles and responsibilities in a contract manufacturing arrangement, see FDA guidance document *Contract Manufacturing Arrangements for Drugs: Quality Agreements at* *http://www.fda.gov/downloads/drugs/guidances/ucm353925.pdf*

Conclusion
Violations cited in this letter are not intended as an all-inclusive list. You are responsible for investigating these violations, for determining the causes, for preventing their recurrence, and for preventing other violations in all your facilities.

Correct the violations cited in this letter promptly. Failure to promptly correct these violations may result in legal action without further notice including, without limitation, seizure and injunction. Unresolved violations in this warning letter may also prevent other Federal agencies from awarding contracts.

Until these violations are corrected, we may withhold approval of pending drug applications listing your facility. We may re-inspect to verify that you have completed your corrective actions. We may also refuse your requests for export certificates.

After you receive this letter, respond in writing within fifteen (15) working days. Specify what you have done since our inspection to correct your violations and to prevent their recurrence. If

you cannot complete corrective actions within 15 working days, state your reasons for delay and your schedule for completion.

Please address your reply to:

Brian D. Garthwaite, Ph.D., Compliance Officer
U. S. Food and Drug Administration
Division of Pharmaceutical Quality Operations III
Minneapolis Office
250 Marquette Avenue, Suite 600
Minneapolis, MN 55401-2142

Refer to the Unique Identification Number (Case# 515029) when replying. If you have questions regarding the contents of this letter, please contact Dr. Brian Garthwaite by phone at (612) 758-7132 or by email at Brian.Garthwaite@fda.hhs.gov.

Sincerely,
/S/

Art O. Czabaniuk
Division Director
Division of Pharmaceutical Operations III