Clover Custom Blending LLC 2/28/18

U.S. FOOD & DRUG ADMINISTRATION

Office of Pharmaceutical Quality Operations,
Division II
4040 N. Central Expressway, Suite 300
Dallas, Texas 75204

February 28, 2018

CMS Case #527994

WARNING LETTER

VIA UPS
Cavan R. Canavan, Sr.
CEO & President
Clover Custom Blending LLC
6205 Johns Rd., Ste. 9
Tampa, FL 33634-4492

Dear Mr. Canavan:

The U.S. Food and Drug Administration (FDA) inspected your drug manufacturing facility, Clover Custom Blending (FEI #3010167039), at 6205 Johns Road, Suite 9, Tampa, FL, from May 15 to 17, 2017.

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

Because your methods, facilities, or controls for manufacturing, processing, packing, or holding do not conform to CGMP, your drug products are 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).

In addition, your firm also manufactures a misbranded drug in violation of the FD&C Act under section 502(c), 21 U.S.C. 352(c).

We reviewed your June 7, 2017, response in detail.

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

1. 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).

You released sunscreen lotion SPF 30 lot # MB170104 which failed to meet established potency specifications for each of the product's three active ingredients.

Active Ingredient	Specification	Your Contract Test Laboratory Result	Potency
Octinoxate	**(b)(4)** to **(b)(4)**%	**(b)(4)**%	Super-Potent
Oxybenzone	**(b)(4)** to **(b)(4)**%	**(b)(4)**%	Super-Potent
Octocrylene	**(b)(4)** to **(b)(4)**%	**(b)(4)**%	Sub-Potent

During the inspection, you stated to our investigator that you believed the out-of-specification results (OOS) were due to a contract laboratory error. However, you did not initiate an investigation to determine the root cause of the OOS results before you released the batch.

In your response, you said you would draft an SOP for handling future OOS results. Your response is inadequate. You did not provide the SOP, nor did you provide evidence to demonstrate that you have investigated these or other OOS results to determine the root cause. You have not evaluated all other batches of sunscreen lotion that may be affected and may have active ingredient levels above or below the range specified for the product. You also have not implemented appropriate corrective actions to prevent recurrence of the laboratory error or the release of sub- or super-potent product.

In response to this letter, provide a summary report of your investigation of any batches that have failed to meet specifications. Include your root cause analysis, explain the scope of the problem, indicate your corrective actions, and describe the preventive actions you have implemented or will implement, along with expected dates of completion.

2. Your firm failed to establish written responsibilities and procedures applicable to the quality control unit. (21 CFR 211.22(d)).

You failed to establish written procedures for multiple over-the-counter (OTC) drug product manufacturing operations, including, but not limited to, training, completion of master batch records, recalls, complaints, deviations, and investigations. Additionally, your quality unit failed to ensure that batch records were complete and included required documentation, such as initials and dates for each step of the operation completed, yield calculations, an example of the label used in each batch, and handwritten or electronic approval signatures.

In your response, you stated that you would create new procedures for several areas, including out-of-specification investigations and complaint investigations, but you did not provide the procedures. In response to this letter, provide your procedures detailing the responsibilities of your quality control unit. Also include your written procedures for creation of master batch records, recalls, complaint handling, and handling of deviations and OOS investigations.

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

Your firm uses the same mixing tank, mixers, and hoses to manufacture OTC topical drug products, **(b)(4)**, and **(b)(4)**. It is unacceptable as a matter of CGMP to continue manufacturing topical drugs using the same equipment that you use to manufacture industrial-grade products, including those that contain known skin irritants.

Our investigator observed a mixer motor, used to mix drug products in open tanks, covered in flaking paint. The investigator also observed a scale, used for weighing raw materials, covered in an unknown white powder and splattered with an unknown yellow liquid. You had no written cleaning procedures or documentation to show that this non-dedicated manufacturing equipment was cleaned between production of industrial-grade products and OTC drugs. You did not demonstrate that you maintained adequate separation to prevent the substances observed on your mixed-use equipment from contaminating your OTC topical drugs with ingredients from your non-pharmaceutical products.

In your response, you stated you would draft cleaning procedures for equipment and manufacturing areas. Although we acknowledge that you cleaned the manufacturing area and equipment during the inspection, your response is inadequate because you did not address the potential for cross-contamination posed by the manufacture of non-pharmaceutical products on the same equipment used to manufacture OTC drug 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.

4. Your firm failed to conduct at least one test to verify the identity of each component of a drug product. Your firm also failed to establish the reliability of component supplier analyses on which you rely in lieu of certain tests through appropriate validation of the supplier's test results at appropriate intervals (21 CFR 211.84(d)(1)&(2)).

You do not test each incoming component of your OTC sunscreen drug products for identity prior to using components in your drug manufacturing process. You also failed to establish the reliability of your suppliers' analyses, and to test each component for conformity with all appropriate written specifications for purity, strength, and quality. You stated during the inspection that you review certificates of analysis (COA) only for incoming API, and you lacked a procedure for the acceptance of incoming components.

In your response, you stated, "We have written SOP's to control and record samplings of each batch of our Active Pharmaceutical Ingredients contracted with a FDA laboratory to do **(b)(4)** testing on our API's to ensure they meet the specifications of our requirements." (*sic.*)

Your response is inadequate. You must test each component to verify its identity. You must also test all components, including active ingredients and inactive ingredients, for conformity with all appropriate written specifications for purity, strength, and quality. If you intend to rely on your suppliers' COA in lieu of such testing, you must still conduct at least an identity test on each component. You must also periodically validate each supplier's test results.

In your response, you did not clearly indicate that you will conduct an identity test on each component, nor have you shown how you will validate the test results of each supplier upon whose COA you intend to rely. Finally, you did not address the potential effects of your failure to conduct incoming component testing on the quality of products you have distributed in the United States that remain within expiry.

In response to this letter, provide a detailed description of how you plan to test each component for conformity with all appropriate written specifications for identity, purity, strength, and quality. If you accept your suppliers' COA in lieu of testing, describe in detail how you plan to establish the reliability of your suppliers' test results through periodic validation. Lastly, provide a risk assessment for any drugs within expiry and distributed within the United States that were manufactured from inadequately tested and controlled components.

Misbranding Charges

Based on the information collected during the inspection, you manufacture the following finished product: Bulk SPF 30 Sunscreen Tote, a bulk container shipped for labeling and repackaging. The label for Bulk SPF 30 Sunscreen Tote includes the following claim that demonstrates the intended use of the product. This is not an inclusive list of all claims demonstrating the product's intended use:

From the product label: "SPF 30"

Based on the above label claim, Bulk SPF 30 Sunscreen Tote is a drug as defined by section 201(g)(1)(B) of the FD&C Act, 21 U.S.C. 321(g)(1)(B), because it is intended for the diagnosis, cure, mitigation, treatment, or prevention of disease, and/or under section 201(g)(1)(C) of the FD&C Act, 21 U.S.C. 321(g)(1)(C), because it is intended to affect the structure or any function of the body of man. Specifically, this product is intended for use to help provide protection from sunburn.

Furthermore, as a finished OTC drug product, the Bulk SPF 30 Sunscreen Tote once introduced into interstate commerce for repackaging, unless exempted under 21 CFR 201.150, must meet all drug labeling requirements described in section 502(c) of the FD&C Act, 21 U.S.C. 352(c) and in 21 CFR 201, including the "Drug Facts" labeling requirements under 21 CFR 201.66. Based on documentation collected there is no evidence that the operators of the establishments where the drugs are to be repackaged are part of Custom Clover Blending LLC., nor is there evidence that there are labeling and repackaging agreements in place with such operators, and, in turn, neither exemption under 21 CFR 201.150(1) or (2), respectively, are met. Therefore, Bulk SPF 30 Sunscreen Tote is misbranded under section 502(c) of the FD&C Act because none of the outer container labeling contains "Drug Facts" required by 21 CFR 201.66.

The introduction or delivery for introduction of a misbranded drug into interstate commerce is prohibited under section 301(a) of the FD&C Act, 21 U.S.C. 331(a). Therefore, the marketing of Bulk SPF 30 Sunscreen Tote violates this provision of the FD&C Act.

CGMP consultant recommended

Based upon the nature of the violations we identified at your firm, we strongly recommend engaging a consultant qualified as set forth in 21 CFR 211.34, to assist your firm in meeting CGMP requirements. Your use of a consultant does not relieve your firm's obligation to comply with CGMP. Your firm's executive management remains responsible for fully resolving all deficiencies and ensuring ongoing CGMP compliance.

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.

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 to this office in writing within 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. Your written notification should refer to the Warning Letter Number above (CMS Case # 527994).

Please address your reply to John W. Diehl, Director, Compliance Branch at the FDA address provided on the first page of this letter. In addition, please submit a signed copy of your response on your firm's letterhead to **ORAPHARM2_CORRESPONDENCE@fda.hhs.gov (mailto:ORAPHARM2_CORRESPONDENCE@fda.hhs.gov)**.

If you have questions regarding the contents of this letter, please contact Dayna I. Martínez at (787) 729-8608 or **dayna.martinez@fda.hhs.gov (mailto:dayna.martinez@fda.hhs.gov)**.

Sincerely,
/S/
Monica R. Maxwell
Program Division Director
Office of Pharmaceutical Quality Operations Division II

CC:

Mary L. Mayleben, Pharm.D.
Pharmaceutical Program Manager
Division of Drugs, Devices and Cosmetics
Department of Business and Professional Regulation
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