Avalon Packaging - Warning Letter - Letter Issued: 11/08/2018

CMS 555500

WARNING LETTER

November 8, 2018

Via UPS Overnight

Ref: #HAF4W-19-03-WL

Mr. Scott A. Barclay, Owner

Avalon Packaging

125 E Main St #603

American Fork, UT 84003-2407

Dear Mr. Barclay:

From March 12, to March 26, 2018, the U.S. Food and Drug Administration (FDA or we) conducted an inspection of your facility located at 50 N Geneva Road, Orem, Utah. During our inspection, FDA collected three raw kratom material samples intended for use in your finished dietary supplement products containing kratom. Based on the inspection and the samples collected during the inspection, we have identified serious violations of the Federal Food, Drug, and Cosmetic Act (the Act) and applicable regulations. You may find the Act and FDA regulations through links on FDA's website at www.fda.gov.

Pathogen Findings

During our inspection, FDA collected three raw kratom material samples intended to be used in your finished dietary supplement products containing kratom, which isolated several serotypes of Salmonella, a human pathogen. Based on the analytical results, these products are adulterated under section 402(a)(1) [21 U.S.C. § 342(a)(1)] of the Act, because they bear or contains a poisonous or deleterious substance which may render them injurious to health.

Salmonella is a pathogenic organism that can cause serious and sometimes fatal infections in young children, frail or elderly people, and others with weakened immune systems. Healthy individuals may suffer short-term symptoms such as severe diarrhea, bloody diarrhea, fever, chills, abdominal discomfort, and occasionally vomiting. FDA laboratory analysis of the three raw ingredient samples of kratom (Sample 1031137 of Red Maeng Da Kratom, 1031138 of White Maeng Da Kratom, and 1031139 of Green Maeng Da Kratom), collected on March 13, 2018, isolated several *Salmonella spp* in all three samples.

Whole Genome Sequencing (WGS) analysis was conducted on the *Salmonella spp* isolates obtained from the three-raw ingredient kratom samples and WGS isolated thirteen (13) different strains of *Salmonella* in the three samples. WGS analysis of bacterial human pathogens provides high-resolution data, enabling links to be established between clinical isolates and food or environmental sources of bacterial contamination and illness. WGS data can also be used to infer the evolutionary relationships (or phylogeny) within a given set of isolates as it measures each DNA position in a bacterial genome. At this time, the comparison of WGS from the *Salmonella* isolates found in the raw ingredient kratom samples shows thirteen (13) strains of *Salmonella* present in the three samples:

1. Red Maeng Da Kratom:

   - A *Salmonella* 14[5]12:b:- strain was isolated from your Red Maeng Da Kratom.
   - A *Salmonella* Javiana strain was isolated from your Red Maeng Da Kratom. Comparing this strain to the larger WGS database shows it is genetically identical to a clinical isolate.
   - A second *Salmonella* Javiana strain was isolated from your Red Maeng Da Kratom.
   - A *Salmonella* Wandsworth strain was isolated from your Red Maeng Da Kratom. Comparing this strain to the larger WGS database shows it is genetically identical to *Salmonella* found in akratom product sample from another kratom processor and a clinical isolate.

2. White Maeng Da Kratom:

   - A *Salmonella* Okatie strain was isolated from your White Maeng Da Kratom. Comparing this strain to the larger WGS database shows it matches isolates from two (2) other Kratom processors and seven (7) clinical isolates, two (2) of which are included in CDC's outbreak definition for a multistate outbreak of Salmonellosis linked to consumption of kratom.
   - A *Salmonella* Thompson strain was isolated from your White Maeng Da Kratom.
   - A second *Salmonella* Thompson strain was isolated from you White Maeng Da Kratom. Comparing this strain to the larger WGS database shows it is genetically identical to a clinical isolate, to the exclusion of all other firms.
   - A *Salmonella* Wandsworth strain was isolated from your White Maeng Da Kratom. Comparing this strain to the larger WGS database shows that it is genetically identical to a kratom product sample collected from another kratom processor.
   - A *Salmonella* Kumasi strain was isolated from your White Maeng Da Kratom.

3. Green Maeng Da Kratom:

   - A *Salmonella* Okatie strain was isolated from your Green Maeng Da Kratom. Comparing this strain to the larger WGS database shows that it matches isolates from five (5) other kratom processors and ten (10) clinical isolates. These clinical isolates are included in CDC's outbreak definition for a multistate outbreak of Salmonellosis linked to consumption of kratom.
   - A *Salmonella* Virchow strain was isolated from your Green Maeng Da Kratom.
   - A *Salmonella* Weltevreden strain was isolated from your Green Maeng Da Kratom.
   - A second *Salmonella* Weltevreden strain was isolated from your Green Maeng Da Kratom.

We acknowledge that you voluntarily destroyed kratom from your facility in response to the outbreak and recalled all kratom products which had been distributed by your company.

Dietary Supplements CGMP Violations

Our inspection found that you have serious violations of the Current Good Manufacturing Practice (CGMP) regulations for Manufacturing, Packaging, Labeling, or Holding Operations for Dietary Supplements, Title 21, Code of Federal Regulations (CFR), Part 111 (21 CFR 111). These violations cause the dietary supplements you manufacture and distribute including, but not limited to: **(b)(4)** Kratom, **(b)(4)**, NXTGEN™ Botanicals

Maeng Da Kratom, and **(b)(4)** to be adulterated within the meaning of section 402(g)(1) [21 U.S.C. § 342(g)(1)] of the Act because the products have been prepared, packed, or held under conditions that do not meet the CGMP regulations for dietary supplements. Introducing or delivering these products for introduction into interstate commerce violates the Act.

During the inspection, you indicated that you were not aware of the CGMP requirements for dietary supplements. We have reviewed your written response dated April 13, 2018, concerning our investigators' observations cited on the Form FDA-483, Inspectional Observations, issued to you on March 26, 2018. Our comments regarding the adequacy of the actions you took or are taking to correct the objectionable conditions and practices observed during the inspection are detailed after the applicable violations, noted below.

Your significant violations are as follows:

1. You failed to establish and follow written procedures for the responsibilities of the quality control operations, including written procedures for conducting a material review and making a disposition decision, and for approving or rejecting any reprocessing, as required by 21 CFR 111.103. Specifically, you did not establish written procedures for the responsibilities of the quality control operations. Once you have established the foregoing, you must make and keep a record of these written procedures, per 21 CFR 111.140(b)(1). Furthermore, you must make and keep a record of written documentation, at the time of performance, that quality control personnel performed the review, approval, or rejection requirements, per 21 CFR 111.140(b)(2).

We have reviewed your response, received on April 13, 2018. Your response stated that you will be taking several actions to address the observation. However, you did not provide supporting documentation with your response. Hence, we are unable to evaluate the adequacy of your corrective actions. We will evaluate the adequacy of your corrective actions at our next inspection

2. You failed to establish specifications for any points, steps, or stages in the manufacturing process where control is necessary to ensure the quality of the dietary supplement and that the dietary supplement is packaged and labeled as specified in the master manufacturing record, as required by 21 CFR 111.70(a).

For example, you failed to establish the following component specifications for each component that you use in the manufacture of a dietary supplement:

- Identity specification [21 CFR 111.70(b)(1)];
- Component specifications that are necessary to ensure that specifications for the purity, strength, and composition of dietary supplements manufactured using the components are met [21 CFR 111.70(b)(2)]; and
- Specifications that establish the limits on those types of contamination that may adulterate or may lead to adulteration of the finished batch of the dietary supplement to ensure the quality of the dietary supplement [21 CFR 111.70(b)(3)].

Further, you failed to establish specifications for each finished dietary supplement that you manufacture for the identity, purity, strength, and composition of the finished batch of dietary supplement and for limits on those types of contaminates that may adulterate, or that may lead to adulteration of, the finished batch of the dietary supplement [21 CFR 111.70(e)].

We have reviewed your response dated April 13, 2018, with the proposed corrective actions for addressing the development of all component, in-process, and finished product specifications within 120 days. Further, your proposed action plan states that you will base your component testing on outcomes, either positive or negative for each component. You also indicated in your response that you will rely on your suppliers' certificates of analysis (COA) to meet the requirements of 21 CFR 111.75 through the use of a Distribution of Responsibilities agreement. In order to rely on a COA to determine that the component specifications have been met, you must comply with the requirements in 21 CFR 111.75(a)(2)(ii), including qualify the supplier in accordance with 21 CFR 111.75(a)(2)(ii)(A). Because your response did not address how you will meet the requirements of 21 CFR 111.75(a)(2)(ii) for relying on a COA from the supplier, we cannot evaluate the adequacy of this corrective action. We will evaluate the adequacy of your corrective actions at our next inspection.

3. You failed to prepare and follow a written master manufacturing record (MMR) for each unique formulation of dietary supplement that you manufacture, and for each batch size, to ensure uniformity in the finished batch

from batch to batch as required by 21 CFR 111.205(a). During the inspection, you told the investigator that you were not aware of the requirement to prepare an MMR for each unique dietary supplement formulation.

Further, for those MMRs which you have developed, you failed to include all required elements per 21 CFR 111.210. Specifically, the MMRs for **(b)(4)**, **(b)(4)**, and NXTGEN™ Botanicals Maeng Da Kratom (Lot 171474) failed to include:

- A statement of theoretical yield of a manufactured dietary supplement at each point, step, or stage of the manufacturing process where control is necessary to ensure the quality of the dietary supplement, and the expected yield when you finish manufacturing the dietary supplement, including the maximum and minimum percentages of theoretical yield beyond which a deviation investigation of a batch is necessary and material review is conducted and disposition decision is made [21 CFR 111.210(f)];
- Specifications for each point, step, or stage in the manufacturing process where control is necessary to ensure the quality of the dietary supplement and that the dietary supplement is packaged and labeled as specified in the MMR [21 CFR 111.210(h)(1);
- Procedures for sampling and a cross-reference to procedures for tests or examinations [21 CFR 111.210(h)(2);
- Specific actions necessary to perform and verify points, steps, or stages in the manufacturing process where control is necessary to ensure the quality of the dietary supplement and that the dietary supplement is packaged and labeled as specified in the MMR [21 CFR 111. 210(h)(3)]; and
- Corrective action plans for use when a specification is not met [21 CFR 111.210(h)(5)].

We have reviewed your response dated April 13, 2018, regarding your MMRs. We cannot verify the adequacy of your response because you failed to include a complete MMR that addresses all required elements. We will evaluate the adequacy of your corrective actions at our next inspection.

4. You failed to include the complete information relating to the production and control of each batch in the batch production record (BPR) as required by 21 CFR 111.255(b). Specifically, the BPR's for **(b)(4)** failed to include all the required elements specified under 21 CFR 111.260.

We have reviewed your response dated April 13, 2018, regarding the BPRs and have concluded that the response is inadequate because the records you supplied failed to include all required elements in the BPRs. Specifically, the Blending Batch Record lacks required information for the cleaning, maintenance, and sanitizing of the **(b)(4)** Blender, including cleaning operations between batches of products, in accordance with 21 CFR 11.260(c). We will evaluate the adequacy of your corrective actions at our next inspection.

New Dietary Ingredient

As an herb or other botanical, kratom is a dietary ingredient under section 201(ff)(1)(C) of the Act [21 U.S.C. § 321(ff)(1)(C)]. Further, as a dietary ingredient that was not marketed in the United States before October 15, 1994, Kratom (mitragyna speciosa) is a "new dietary ingredient" under section 413(d) of the Act [21 U.S.C. § 350b(d)].

Under section 413 of the Act [21 U.S.C. §350b], a dietary supplement that contains a new dietary ingredient (i.e., a dietary ingredient not marketed in the United States before October 15, 1994) shall be deemed adulterated under section 402(f) of the Act [21 U.S.C. § 342(f)] unless it meets one of two requirements:

1. The dietary supplement contains only dietary ingredients that have been present in the food supply as an article used for food in a form in which the food has not been chemically altered; or

2. There is a history of use or other evidence of safety establishing that the dietary ingredient when used under the conditions recommended or suggested in the labeling of the dietary supplement will reasonably be expected to be safe and, at least 75 days before being introduced or delivered for introduction into interstate commerce, the manufacturer or distributor of the dietary ingredient or dietary supplement provides FDA with information, including any citation to published articles, which is the basis on which the manufacturer or distributor has concluded that a dietary supplement containing such dietary ingredient will reasonably be expected to be safe.

To the best of FDA's knowledge, there is no information demonstrating that kratom was lawfully marketed as a dietary ingredient in the United States before October 15, 1994, nor is there information demonstrating that this

ingredient has been present in the food supply as an article used for human food in a form in which the food has not been chemically altered. In the absence of such information, kratom is subject to the notification requirement in section 413(a)(2) of the Act [21 U.S.C. § 350b(a)(2)] and 21 CFR 190.6. Because the required notification has not been submitted, your products are adulterated under sections 402(f)(1)(B) and 413(a) of the Act [21 U.S.C. §§ 342(f)(1)(B) and 350b(a)].

Even if the required notification had been submitted, we know of no evidence that would establish that your kratom products are not adulterated. In the absence of a history of use or other evidence of safety establishing that kratom, when used under the conditions recommended or suggested in the labeling of your products, will reasonably be expected to be safe, your **(b)(4)** Kratom and NXTGEN™ Maeng Da Kratom products are adulterated under sections 402(f)(1)(B) and 413(a) of the Act [21 U.S.C. §§ 342(f)(1)(B) and 350b(a)] because they contain a new dietary ingredient for which there is inadequate information to provide reasonable assurance that such ingredient does not present a significant or unreasonable risk of illness or injury. Introduction of such products into interstate commerce is prohibited under section 301(a) and (v) of the Act [21 U.S.C. §§ 331(a) and (v)]. To the best of FDA's knowledge, there is no history of use or other evidence of safety establishing that kratom will reasonably be expected to be safe when used as a dietary ingredient.

The FDA recognizes that your firm voluntarily destroyed **(b)(4)** kg of kratom product on March 13, 2018.

The violations cited in this letter are not intended to be an all-inclusive list of the violations that exist at your facility or in connection with your products. 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 the Act and all implementing regulations. You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations may result in enforcement action by the FDA without further notice, including seizure and/or injunction.

Section 743 of the Act [21 U.S.C. § 379j-31] authorizes FDA to assess and collect fees to cover FDA's costs for certain activities, including re-inspection-related costs. A re-inspection is one or more inspections conducted subsequent to an inspection that identified noncompliance materially related to a food safety requirement of the Act, specifically to determine whether compliance has been achieved. Re-inspection related costs mean all expenses, including administrative expenses, incurred in connection with FDA's arranging, conducting, and evaluating the results of the re-inspection and assessing and collecting the re-inspection fees [21 U.S.C. § 379j-31(a)(2)(B)]. For a domestic facility, FDA will assess and collect fees for re-inspection related costs from the responsible party for the domestic facility. The inspection noted in this letter identified noncompliance materially related to a food safety requirement of the Act. Accordingly, FDA may assess fees to cover any re-inspection related costs.

Please respond to this office in writing within fifteen (15) working days of the receipt of this letter as to the specific steps you are taking to correct the stated violations, including an explanation of each step to identify violations and make corrections to ensure that similar violations will not occur. In your response, you should include documentation, including revised procedures, photographs, results of tests you have conducted, and any other useful information that would assist us in evaluating your corrections. If you do not believe that your products are in violation of the Act, include your reasoning and any supporting information for our consideration. If the corrective action cannot be completed within fifteen working days, state the reason for the delay and the time frame within which the corrections will be implemented.

Your reply should be addressed to the U.S. Food and Drug Administration, Attn: Hanna L. Potter, Compliance Officer, 6th Ave & Kipling St, DFC - Bldg 20, PO Box 25087, Denver, Colorado 80225-0087. You may reach Ms. Potter at (303) 236-3094 if you have any question about this matter.

Sincerely,

/S/

LaTonya M. Mitchell

Program Division Director

Office of Human and Animal Foods -

Division IV West

cc: Richard Beckstrand

Manufactured Food Program Manager

Regulatory Services

Utah Department of Agriculture

350 North Redwood Rd

Salt Lake City, UT 84116

