U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR FOOD SAFETY & APPLIED NUTRITION

April 28, 2021

Mr. Kevin M. Bell
Partner
Arnall Golden Gregory LLP
1775 Pennsylvania Avenue NW, Suite 1000
Washington, DC 20006

Dear Mr. Bell:

We are writing to respond to your February 24, 2020, letter (February 2020 letter) to Steven Tave, former Director of the Office of Dietary Supplement Programs (ODSP) at the Food and Drug Administration (FDA or the Agency), "request[ing] that FDA take swift and appropriate enforcement action against companies that are importing adulterated beta-alanine into the United States in clear violation of the Federal Food, Drug & Cosmetic Act." In your February 2020 letter, you assert that (1) " . . . the majority of beta-alanine imported into the United States is generic and does not rely on a [new dietary ingredient notification] NDIN, and as such is adulterated under Section 402(f)," and (2) "[t]here are numerous inherent and unnecessary risks to the public health by continuing to allow the use of generic beta-alanine in dietary supplements." We appreciate your continued engagement with FDA as we have evaluated this issue.[1] We have carefully considered the information you provided as well as other information available to the Agency, and we do not agree that there is clear evidence to support either assertion.

With regard to your first assertion that " . . . the majority of beta-alanine imported into the United States is generic and does not rely on a [new dietary ingredient notification] NDIN, and as such is adulterated under Section 402(f)," for purposes of this response, we interpret your use of "generic" to mean that the beta-alanine that you assert is adulterated is not the same beta-alanine that is the subject of the NDIN submitted by Natural Alternatives International, Inc. (NAI). We do not dispute your assertion that beta-alanine is being imported into the United States that is not the subject of NAI's NDIN; however, the fact that a dietary ingredient is not covered by NAI's NDIN, or any NDIN, does not automatically render the dietary ingredient adulterated under section 402(f) of the Federal Food, Drug & Cosmetic Act (FD&C Act).

[1] This response also captures the substance of, and addresses some of the issues raised during, a March 31, 2021, call between you and Dr. Daniel Fabricant from the Natural Products Association and FDA representatives from the Center for Food Safety and Applied Nutrition's Office of the Center Director, Office of Compliance, and ODSP, as well as FDA's Office of the Chief Counsel.

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For a dietary supplement to be deemed adulterated under section 402(f) of the FD&C Act for failure to meet the requirements in section 413(a) of the FD&C Act, the dietary supplement must, as a threshold matter, contain a "new dietary ingredient" as defined in section 413(d) of the FD&C Act, and it must not be exempt from the requirement to submit a new dietary ingredient notification under section 413(a)(1) of the FD&C Act. Section 413(a)(1) of the FD&C Act exempts from the new dietary ingredient notification requirement a "dietary supplement which contains only dietary ingredients which 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." While the NDIN process set forth in section 413(a) provides a powerful tool to FDA to be able to evaluate the safety of certain new dietary ingredients contained in dietary supplements, before asserting that a dietary supplement containing a new dietary ingredient is deemed adulterated under sections 413(a) and 402(f), FDA bears the burden of establishing that the requirement to submit an NDIN applies.

Importantly, to meet this burden, FDA would need to demonstrate that beta-alanine is not present in the food supply as an article used for food in a form in which the food has not been chemically altered. In reviewing NDINs, FDA focuses on confirming that the information submitted demonstrates the safety of the ingredient when used under the conditions recommended or suggested in the labeling. 21 CFR 190.6(b) specifies the information that must be included in the notification, but such information does not necessarily include information demonstrating whether the dietary ingredient has not been present in the food supply as an article used for food in a form in which the food has not been chemically altered (see section 413(a)(1) of the FD&C Act). FDA has reviewed and intends to continue reviewing voluntarily submitted notifications for NDIs that may be exempt from the notification requirement under section 413(a)(1) of the FD&C Act.[2] While our review of the safety information included with NAI's NDIN did not raise any safety concerns, our response should not be interpreted as a conclusion about whether beta-alanine generally is subject to the requirements in section 413(a)(2) of the FD&C Act.

While FDA has not reached a definitive conclusion as to whether beta-alanine would be excepted from the NDI notification process on the grounds that it is present in the food supply as an article used for food in a form in which the food has not been chemically altered, FDA is aware of evidence suggesting that beta-alanine is present in the food supply as, for example, an ingredient in energy drinks. The presence of beta-alanine in the food supply raises significant questions that would need to be answered before FDA would be in a position to demonstrate that certain imported beta-alanine appears to be adulterated.

With regard to your second assertion that "[t]here are numerous inherent and unnecessary risks to the public health by continuing to allow the use of generic beta-alanine in dietary supplements," we are not aware of any evidence to support an assertion that beta-alanine manufactured by others presents a risk to the public health. Your communication speculated as to potential reasons that beta-alanine manufactured by other entities could be adulterated, but it did not provide any specific evidence that other beta-alanine currently being imported into the United States is adulterated. While we acknowledge that differences in manufacturing could potentially change the safety and suitability of the ingredient for certain conditions of use, or

[2] See FDA, Draft Guidance for Industry, Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; August 2016, at 25, Available at https://www.fda.gov/media/99538/download.

even change the identity of the ingredient,[3] FDA is not aware that such differences are at issue here. To the extent you have specific evidence of particular risks of safety or other evidence of adulteration, we welcome the opportunity to review such information. However, speculation about differences in the manufacturing process or about potential contaminants is generally not sufficient to support an enforcement action. Additionally, while we agree that requiring additional information about the manufacturing process for a particular new dietary ingredient prior to its marketing *would* be more helpful in helping to ensure the ingredient's safety, your February 2020 letter essentially sets forth an argument for why the NDI notification requirement *should* be broader than it currently is, rather than explaining what the law currently requires. As explained previously in this letter, we have not identified evidence that FDA could use to demonstrate that beta-alanine generally is subject to the NDI notification requirement in section 413(a)(2). In the absence of such evidence, FDA bears the burden of demonstrating that beta-alanine is adulterated—for example, that it is 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. See section 402(f)(1)(B) of the FD&C Act.

Based on the NDIN we have received as well as other information FDA has reviewed pertaining to beta-alanine generally, we have not identified any information that is sufficient for the Agency to demonstrate that any imported beta-alanine presents a risk to public health or that the safety information available does not also demonstrate the safety of beta-alanine more generally. As you noted in your February 2020 letter and in our March 31 call regarding this issue, FDA did not object to NAI's basis for concluding that its beta-alanine is reasonably expected to be safe. As such, it is unclear on what basis FDA could prove that there is not a reasonable assurance that beta-alanine more generally does not present a significant or unreasonable risk of illness or injury. If a particular beta-alanine were sufficiently different from NAI's beta-alanine such that the prior safety assessment no longer translated, then it might be possible to demonstrate that such beta-alanine would be adulterated under section 402(f)(1)(B) of the FD&C Act. However, this would require affirmative evidence of how this beta-alanine differs, and why those differences alter the safety analysis. We have seen no such evidence here.

To be clear, we are not today asserting definitively that certain imported beta-alanine for use as a dietary ingredient in dietary supplements is not adulterated. However, as noted above, we have significant questions about whether it is. Even assuming that imports of beta-alanine, or certain imports of beta-alanine, were unlawful, FDA makes regulatory and enforcement decisions on a case-by-case basis, recognizing that it is unable, as a practical matter, to take enforcement action against every violative product. FDA needs to make the best use of Agency resources, and we typically prioritize those issues for which there is a known safety risk for consumers. At this time, we do not have concerns about beta-alanine that warrant the further investment of FDA's limited resources. If you have additional information to provide that might change our current

[3] *See, e.g.*, FDA, Draft Guidance for Industry, Dietary Supplements: New Dietary Ingredient Notifications and Related Issues; August 2016, at 20-21, Available at https://www.fda.gov/media/99538/download; FDA, Guidance for Industry: Assessing the Effects of Significant Manufacturing Process Changes, Including Emerging Technologies, on the Safety and Regulatory Status of Food Ingredients and Food Contact Substances, Including Food Ingredients that Are Color Additives; June 2014 Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-assessing-effects-significant-manufacturing-process-changes-including-emerging.

thinking, please let us know. We will continue to monitor the marketplace and, whenever we identify violations of the law, we will take action as appropriate to protect the public health.

Sincerely,

Cara Welch, Ph.D.
Acting Director
Office of Dietary Supplement Programs
Center for Food Safety and Applied Nutrition