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October 28, 2021

Janet Woodcock, MD
Acting Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

Dear Acting Commissioner Woodcock,

I am writing to request a written response to the questions below posed to you regarding the Food and Drug Administration's (FDA) sudden change of policy expressed in warning letters sent to multiple dietary supplement companies regarding the inclusion of N-acetyl cysteine (NAC) in their products.[1]

To gain clarity on the FDA's change in policy regarding the inclusion of NAC in dietary supplements, I demand answers to the following questions:

1. What is the basis for the FDA's sudden change in its long-standing policy on the inclusion of NAC in the formulation of dietary supplement products (setting aside the use of impermissible therapeutic claims that would appropriately restrict the marketing of products containing NAC on that basis)?
2. The National Institute of Health (NIH) Office of Dietary Supplements stated that during the COVID-19 pandemic, "No safety concerns have been reported for products labeled as dietary supplements that contain NAC."[2] Please provide my office with a complete list of every serious adverse event report submitted to the FDA that has resulted from consumer use of products containing NAC.
3. The FDA's Dietary Supplement website appears to present confusing and possibly inaccurate information on the date at which NAC was first identified or designated as a drug. Those inaccuracies raise a question as to whether the drug exclusion criteria under the Dietary Supplement Health and Education Act (DSHEA) would preclude NAC from being included as an ingredient in a dietary supplement. Please provide a response to the FDA's position on the following issues:

[1]FDA Sends Warning Letters to Seven Companies Illegally Selling Hangover Products. (July 29, 2020). https://www.fda.gov/food/cfsan-constituent-updates/fda-sends-warning-letters-seven-companies-illegally-selling-hangover-products

[2]NIH Office of Dietary Supplements, Dietary Supplements in the Time of COVID-19. (October 5, 2021). https://ods.od.nih.gov/factsheets/COVID19-HealthProfessional/

a. How many structure/function claim notifications for NAC products have been submitted to the FDA for review and how many new dietary ingredient notifications (NDINs) for NAC products have been submitted to the FDA review? Of those, how many did the FDA determine to be inappropriate for marketing?

b. How many enforcement actions did the FDA take to address the marketing of NAC products by companies attempting to receive an NDIN for those products?

c. In a 2016 review of a qualified health claim application by Sevo Neutraceuticals the FDA characterized NAC as a "nutritional substance."[3] In contrast to this characterization, the FDA alleged in its 2020 warning letters that NAC is a drug that was approved prior to the passage of DSHEA and therefore cannot be marketed as a dietary supplement or a nutritional substance. How does the FDA reconcile the contradiction between these two characterizations of NAC?

d. What was the specific date at which the FDA identified NAC was being used in consumer products in the United States, both as a drug and as a dietary supplement or dietary ingredient?

    i. In your response, please also provide an analysis of the composition of the NAC present in the application for approval as a drug at that time and the composition of NAC as a dietary supplement at that time.

    ii. Please also provide all documents supporting the FDA's approval of NAC as a drug. In addition, please provide the Orange Book listing of any drug showing NAC as an active ingredient on the date in the 1960s that the FDA purports it approved the drug.

e. DSHEA was not intended to allow the FDA to remove products marketed as supplements from the marketplace in order to create an arguable advantage for any company marketing a drug with a previously used dietary supplement, such as NAC, as the active ingredient. Given this, what is the FDA's position on whether NAC should be banned from formulated dietary supplements under DSHEA's drug exclusion criteria?

f. I have been told that records have been submitted to the FDA demonstrating that NAC was safely on the market prior to the passage of DSHEA. Does the FDA believe the intent of DSHEA is to remove products that were safely on the market prior to 1994?

g. Does the FDA intend to remove from consumer access the more than 1,170 products containing NAC that are listed on the NIH's Dietary Supplement Label Database?

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[3] Petition for a Qualified Health Claim for a Nutraceutical Formulation and Management of Behavior and Cognitive Difficulties that Can Accompany Dementia. (Docket No. FDA-2016-Q-1523). https://www.fda.gov/media/119441/download (Accessed August 22, 2021).

Additionally, there has been much discussion by the FDA of a re-envisioned regulatory framework. In the FY20 budget request, FDA provided language that spelled out their proposal to "Strengthen FDA's Implementation and Enforcement of DSHEA." The language provides recaps the market growth and acknowledges "FDA is not currently authorized to require a listing of dietary supplement products on the market and has no mechanism in place to complies such basic information about those products. The proposal would require all products marketed as 'dietary supplements to be listed with FDA and give FDA the authority to act against non-compliant products and the manufacturers and distributors of such products."

However, FDA already has access to essential information about products. As referenced in a recent Congressional Research Service report, the NIH, FDA, and DoD provide consumers with dietary supplement information. The NIH Office of Dietary Supplements maintains two databases, one for labels and another for ingredients that provide information on dietary supplements. In fact, the dietary supplement label database was recently updated and included more than 130,000 labels. Additionally, FDA has other tools at their disposal delimitated to them by DSHEA and the Food Safety Modernization Act (FSMA), including good manufacturing (GMP) inspections to go after bad actors. FSMA was designed to make the FDA more proactive than reactive to food safety problems. One mandate included in FSMA was that FDA increases the frequency of its inspections of domestic food facilities based on risk. All facilities that manufacture, process, pack, and store food must register the facility with the FDA. With this in mind, I am demanding written answers to the following questions:

1. The purpose of an import alert is to (i) prevent potentially violative products from being distributed in the United States, (ii) free-up agency resources to examine other shipments, (iii) provide uniform coverage across the country, and (iv) place the responsibility back on the importer to ensure that the products being imported into the United States comply with the FDA's laws and regulations. How has the agency fully utilized the import alerts and bulletins to ensure imported products comply with the FDA's laws and regulations, such as new dietary ingredient notifications?

2. During the May 16, 2019, Responsible Innovation in Dietary Supplements Public Meeting hosted by the FDA, acting Commissioner Sharpless stated the industry has grown to include an estimated 80,000 products. Therefore, the frequency of bad actors exporting potentially and likely violative ingredients into the United States is likely significant. Yet, despite this, the agency has issued only two import alerts in the last six years. If the agency does not utilize import alerts and bulletins, and inspections have decreased over several years. How is the FDA ensuring products entering the United States from countries like China comply with our laws?

3. In 2019 and 2020, the Office of Dietary Supplements was presented with a request that the FDA utilize enforcement action against companies importing adulterated beta-alanine into the United States from China. According to the Natural Alternatives International (NAI), this action would serve the public interest and protect dietary supplement brand owners that invest resources necessary to submit a new dietary ingredient notification (NDIN) to the FDA. Under FDA's final rule, *Premarket Notification for a New Dietary*

Ingredient, 62 Fed. Reg. 49886 (Sept. 23, 1997), if a manufacturer fails to submit the required NDIN to the FDA, a dietary supplement containing an NDI is deemed to be adulterated under Section 402(f). NAI also informed FDA that 2,313,210 kilograms of adulterated beta-alanine were imported from China and under Section 402(f) are adulterated. Despite this, the FDA chose against issuing an import alert or bulletin for adulterated beta-alanine, nor did FDA give a for-cause inspection of these facilities. Thus, these Chinese manufacturers and distributors knowingly evaded federal law by denying the FDA its statutorily mandated opportunity to evaluate the identity and production methods for these forms of beta alanine. How has the FDA determined that Chinese imported beta-alanine is not only safe but not violating US law?

4. NAI provided the FDA with information on their NDIN and identified specific companies manufacturing and importing adulterated beta-alanine into the United States. Has the FDA reviewed these companies to ensure they comply with Section 415 of the FD&C Act (21 U.S.C. 350d), which requires domestic and foreign facilities that manufacture, process, pack, or hold food for human or animal consumption in the United States to register with the FDA?

This matter is of very strong interest to me and my constituents. Therefore, I expect to receive your response with answers no later than November 24, 2021.

Blessings and Libery,

Jeff Duncan
Member of Congress