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July 27, 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, in accordance with Code of Federal Regulations (CFR) Title 21 Part 15 Subpart B,[1] that a public hearing be scheduled to clarify the Food and Drug Administration's position on the use of N-acetyl-L-cysteine (NAC) in dietary supplements.

Last year, the FDA sent warning letters to multiple dietary supplement companies regarding the inclusion of NAC in products utilized to diminish hangovers that result from alcohol intoxication.[2]

NAC has been used as an ingredient in dietary supplements products for decades, and the National Institutes of Health Dietary Supplement Label Database identifies the use of NAC in nearly 1,500 dietary supplement products.[3] Thus, the FDA's recent communications claiming that "NAC products are excluded from the dietary supplement definition under section 201(ff)(3)(B)(i) of the [Federal Food, Drug, and Cosmetic Act] Act [21 U.S.C. § 321(ff)(3)(B)(i)]"[4] is of great concern to many in the dietary supplements industry who seek to provide legal and safe products to consumers and are concerned about the precedent this would set.[5]

[1] 21 CFR15.20 https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=15.20
[2] 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
[3] National Institutes of Health, Dietary Supplement Label Database. (Accessed July 6, 2021). https://dsld.od.nih.gov/dsld/lstIngredients.jsp?list=n
[4] FDA Warning Letter to LES Labs. (July 23, 2020). https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/les-labs-593764-07232020
[5] See for example, Council for Responsible Nutrition Citizen Petition Requesting FDA Allow N-acetyl-L-cysteine (NAC) to be Marketed as a Dietary Supplement, June 1, 2020. https://www.crnusa.org/sites/default/files/Daily/2021-06/CRN%20NAC%20Citizen%20Petition%20--%206.1.21%20Final.pdf

The sudden change of policy expressed in these FDA warning letters conflicts with historical precedent, including that the FDA has permitted NAC to be included as an ingredient in dietary supplement products for decades. To gain clarity on this change in policy, I request that the FDA respond 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 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."[6] 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:

    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."[7] 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?

[6] https://ods.od.nih.gov/factsheets/COVID19-HealthProfessional/
[7] https://www.fda.gov/media/119441/download

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?

As you may know, the dietary supplements industry is the second-largest industry in my home State of Utah, and this matter is of very strong interest to me and my constituents. In addition to answering these questions, scheduling a public hearing would be greatly beneficial as the dietary supplements industry seeks clarity on the FDA's actions regarding NAC. I look forward to receiving your response by Tuesday, August 10, 2021.

Sincerely,

Senator Michael S. Lee