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

November 24, 2021

Steve Mister
Megan Olsen
Council for Responsible Nutrition
1828 L Street, NW, Suite 810
Washington, D.C. 20036-5114

Re: Docket Number FDA-2021-P-0523

Dear Mr. Mister and Ms. Olsen:

This letter is a tentative response to your citizen petition dated June 1, 2021, requesting that the Food and Drug Administration (FDA or we) reverse our "recently adopted position that the Federal Food, Drug, and Cosmetic Act (FDCA) prohibits manufacturers from marketing products containing N-acetyl-L-cysteine (NAC) as dietary supplements." See Citizen Petition from Steve Mister and Megan Olsen, Council for Responsible Nutrition (CRN), submitted to the Division of Dockets Management, FDA, dated June 1, 2021, at page 1.

We are advising you, in accordance with 21 CFR 10.30(e)(2)(iv), that we are currently considering the issues raised by your citizen petition along with the other information filed in the docket, and that we have not reached a decision on your petition because of the complex nature of your request and research that we are still working to complete.

On August 24, 2021, FDA received a second citizen petition, from Daniel Fabricant on behalf of the Natural Products Association (NPA), requesting that "the Commissioner of Food and Drugs either determine, based on the facts provided [in the petition], that [NAC] is not excluded from the definition of a dietary supplement under 21 U.S.C. § 321(ff)(3) or, in the alternative, to recommend and support to the Secretary of HHS, that they issued [sic] a regulation, after notice and comment, finding that NAC, would be lawful under the [FDCA]." See Docket No. FDA-2021-P-0938, Citizen Petition from Daniel Fabricant, NPA, submitted to the Division of Dockets Management, FDA, dated August 18, 2021 (NPA Petition), at page 1. Due to the overlap between your citizen petition and the NPA Petition, we are evaluating both petitions concurrently.

Under section 201(ff)(3)(B) of the FDCA (21 U.S.C. 321(ff)(3)(B)), if an article has been approved as a new drug under section 505 of the FDCA (21 U.S.C. 355), licensed as a biologic under section 351 of the Public Health Service Act (42 U.S.C. 262), or has been authorized for investigation as a new drug or biological for which substantial clinical investigations have been

instituted and for which the existence of such investigations has been made public, then products containing that article are outside the definition of a dietary supplement unless an exception applies. There is an exception if the article was marketed as a dietary supplement or as a food before such approval, licensing, or authorization. To help FDA respond to your petition and the NPA petition, we are open to receiving information from interested parties on the earliest date that NAC was marketed as a dietary supplement or as a food.

In addition, to help us evaluate NPA's request to initiate rulemaking, should we reach this issue, we are asking that interested parties submit information to the NPA docket (FDA-2021-P-0938) regarding the below topics. To ensure that we are able to review all information in a timely manner, we request that submissions be received by January 25, 2022. FDA is committed to reviewing this information expeditiously.

FDA is seeking data, research results, and other information related to the below topics. We ask that interested parties explain their responses and provide any data, evidence, or other information supporting the responses. We also ask that interested parties clearly identify the topic number and subsection, if applicable, associated with their responsive information.

If applicable, FDA intends to use the information submitted to the docket and other appropriate information to inform our thinking as to the appropriateness of using our rulemaking authority under section 201(ff)(3) of the FDCA (21 U.S.C. 321(ff)(3)) with regard to NAC.

A. Data to Assess the Safe Use of NAC as or in a Dietary Supplement

1. Data or information regarding past safe use of NAC in products marketed as dietary supplements. The following are of particular interest:
    i. Product formulations and conditions of use, including, but not limited to, any identifying characteristics of the intended population (e.g., age and sex), duration of use, and frequency of use.
    ii. Sales and marketing data or information in connection with these products, including sales figures, invoices or brochures, and production amounts.
    iii. Data or information regarding consumer complaints or adverse events associated with the use of these products.
    iv. Data or information regarding epidemiological studies or human historical consumption survey results.
2. Other data or information regarding safety with respect to NAC. The following are of particular interest:
    i. Data or information relevant for determination of NAC's toxicity profile, including unpublished and published safety studies and related information relevant to a safety assessment as well as safety studies that identify adverse effects or that bear on the determination of an acceptable daily intake.

ii. Data or information related to human trials or clinical studies intended to evaluate the safety of NAC, specifically trials or studies on healthy individuals that collected safety endpoints and adverse events.

B. Data to Identify Potential Safety Concerns with NAC When Used as or in a Dietary Supplement[1]

1. Data or information as to any conditions or uses under which NAC would present a significant or unreasonable risk of illness or injury.
2. Data or information as to any conditions or uses under which the use of NAC in dietary supplements may render the dietary supplement injurious to health.

We will contact you when our review is complete, at which time we will inform you of the actions, if any, we decide are appropriate in response to your petition.

Sincerely,

Douglas W. Stearn -S Digitally signed by Douglas W. Stearn -S
Date: 2021.11.23 15:49:19 -05'00'

Douglas Stearn
Deputy Director for Regulatory Affairs
Center for Food Safety and Applied Nutrition

[1] Relevant to the applicable provisions of section 402(f)(1) of the FDCA (21 U.S.C. 342(f)(1)), FDA has received information that NAC was marketed as a dietary ingredient in the United States before October 15, 1994.