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FDA Seeks Information on N-acetyl-L-cysteine (NAC)

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- N-acetyl-L-cysteine (NAC) is widely available as a dietary supplement and is also used to treat acetaminophen (Tylenol) poisoning and other conditions, such as lung collapse. In July 2020, the U.S. Food and Drug Administration (FDA) sent warning letters to seven companies about products containing NAC. FDA's July 29, 2020 Constituent Update explains that claims to cure, treat, mitigate, or prevent hangovers make these products unapproved new drugs. Further, as described, for example, in the July 29, 2020 warning letter to LES Labs, even if the product labeling did not have therapeutic claims, which make the products unapproved new drugs, the product could not be lawfully marketed as a dietary supplement because, finding no evidence that NAC was marketed as a dietary supplement or as a food prior to September 14, 1963, when NAC was approved as a new drug, FDA has concluded that NAC products are excluded from the dietary supplement definition under section 201(ff)(3)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (FD&C Act). The definition of a "dietary supplement" specifically excludes articles that are approved as new drugs, certified as antibiotics, or licensed as biologics, or authorized for investigation for therapeutic uses for which "substantial clinical investigations have been instituted and for which the existence of such investigations has been made public" and which were not "marketed as a dietary supplement or as a food" before such approval, certification, or authorization.

- On November 24, 2021, FDA posted a Constituent Update requesting information on the earliest date that NAC was marketed as a dietary supplement or as a food, the safe use of NAC in products marketed as a dietary supplement, and any safety concerns. FDA's public request follows letters issued by FDA in tentative response to two citizens petitions (June 1, 2021 Council for Responsible Nutrition (CRN) petition and August 18, 2021 Natural Products Association (NPA) petition) that ask FDA to reconsider its position on the use of NAC as a dietary supplement. Both petitions characterize FDA's "drug exclusion" position on NAC as a sudden policy change. For example, the CRN petition notes that FDA has "considered over 100 structure-function claim notifications regarding NAC and at least one qualified health claim petition for a dietary supplement containing NAC, and has not objected to the presence of NAC in any of these products." Both petitions ask FDA to distinguish NAC use as a dietary supplement from its use a drug based on the form of administration, i.e., ingestion in the case of a dietary supplement, and intravenous injection or inhalation when used as a drug. The NPA petition additionally asks FDA, alternatively, to initiate discretionary rulemaking to permit NAC as a lawful dietary supplement under the FD&C Act.

- FDA is asking all interested parties to submit the requested information on NAC by January 25, 2022, while FDA continues to evaluate the CRN and NPA citizen petitions. FDA will provide a final response to both petitioners directly once its review is completed. In the event that FDA is not persuaded that the “drug exclusion” does not apply, and there is insufficient safety data to initiate rulemaking that could make certain dietary supplement uses of NAC legal, it remains to be seen whether future FDA warning letters will target NAC-based dietary supplements that do not make drug claims. It is possible that FDA may instead exercise enforcement discretion in the same manner it has for other products, such as cannabidiol (CBD), that are actively marketed as dietary supplements despite FDA’s clear position that the “drug exclusion” applies.

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