July 30, 2020

Mr. Mario Sindaco
Executive Secretariat
The United States Pharmacopeial Convention, Inc.
12601 Twinbrook Parkway
Rockville, MD 20852

REF: 07-20-037-N

Dear Mr. Sindaco,

This letter pertains to the monographs for Alcohol, Dehydrated Alcohol and other related monographs and to a recent meeting between FDA and USP regarding the addition of a Limit Test for Methanol in the Identification section of the monographs. As requested by USP, we are providing written comments for consideration by USP and the Excipient Monographs Expert Committee.

FDA notified USP that the agency has seen an increasing number of hand sanitizer products contaminated with Methanol; we continue to update information on this issue on our public website https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-methanol. As stated on our website, the agency is aware of adults and children ingesting hand sanitizer products contaminated with methanol that has led to recent adverse events, including blindness, hospitalizations and death.

Due to the COVID-19 public health emergency, the use of hand sanitizer products has sharply increased, which broadens the potential exposure of consumers to such products contaminated with Methanol. In addition, since Alcohol and Dehydrated Alcohol are widely used as pharmaceutical ingredients, FDA is concerned that this critical contamination risk is poised to have a broad impact on the supply chain.

As one important step to help address this issue, Agency experts believe that it would be beneficial to include a test for methanol in the "Identification" section of Alcohol, Isopropyl Alcohol and any related USP/NF monographs to help prevent methanol contamination. FDA recommends keeping the methanol limit already required in the Organic Impurities test of USP Alcohol and Dehydrated Alcohol monographs.

From a regulatory standpoint, it makes a difference whether the detection and quantification of Methanol is considered part of the Identification test or is considered part of impurity testing. If Methanol detection and quantification is part of the Identification test, the CGMP regulations at 21 CFR 211.84(d)(1) would require that manufacturers of drug products detect and quantify any Methanol present for each lot of Alcohol received. Furthermore, manufacturers of Alcohol could not deviate from the Methanol limit since this would be an aspect of identity. In contrast, if

Methanol detection and quantification is part of an impurity test, a manufacturer need not include as part of its identity testing the detection and quantification of Methanol in the Alcohol. In addition, a manufacturer could deviate from the impurity requirements established in the monograph by labeling the product to indicate that it deviates from the USP test requirements in this regard. The agency would, however, consider such deviation from the impurity test requirements to render the drug adulterated under the Federal Food, Drug, and Cosmetic Act.

FDA intends to refer manufacturers to the Identification tests in the USP monograph. For the Alcohol and Dehydrated Alcohol monographs, we recommend moving the entire test for the Limit of Methanol from the Organic Impurities section to Identification - Test C. We recommend that USP consider appropriate approaches to introduce this test for the Isopropyl alcohol and any related USP-NF and FCC monographs as well.

Manufacturers should evaluate their supply chain for this product and contact CDER Drug Shortage Staff at drugshortages@fda.hhs.gov if any access or potential drug shortage issues arise. Contacting the Drug Shortages Staff also allows manufacturers to meet any obligations to report discontinuances or interruptions in drug manufacture under 21 U.S.C. § 356C(b) and allows FDA to consider, as soon as possible, what actions, if any, may be needed to avoid shortages and protect the health of patients who depend on the products.

Because this is a current COVID-19 related patient safety issue, we are requesting that this issue be discussed and addressed with urgency. We hope these comments will be helpful to USP and the Excipient Monographs Expert Committee. Please feel free to contact me at pallavi.nithyanandan@fda.hhs.gov if there are any questions. Please use the reference number provided above on any ensuing correspondence.

Sincerely yours,

Pallavi Nithyanandan -S

Digitally signed by Pallavi Nithyanandan -S
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