



Elliot Harrison
Lewis & Harrison
122 C Street, N.W.
Suite 505
Washington, DC 20001

Re: GRAS Notice No. GRN 000770

Dear Mr. Harrison:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000770. We received the notice that you submitted on behalf of Enartis USA, Inc. (Enartis) on March 20, 2018, and filed it on April 19, 2018. Enartis submitted amendments to the notice on July 10, 2018, and July 30, 2018. These amendments include a rewritten Part 6 of the notice,¹ clarification regarding references cited in Part 6, and a statement that Enartis' conclusions are based on the results of published toxicity studies.²

The subject of the notice is potassium polyaspartate for use as a stabilizer preventing tartrate crystal precipitation in wine at levels up to 300 mg/L. The notice informs us of Enartis' view that this use of potassium polyaspartate is GRAS through scientific procedures.

Enartis provides information about the identity and composition of potassium polyaspartate, including a description from the European Food Safety Authority (EFSA).³ Potassium polyaspartate is a potassium salt of a homopolymer of L-aspartic acid with a molecular formula ($C_4H_4NO_3K$)_n, a weight average molecular weight of 5300 g/mol, and is designated by the CAS Registry Number 64723-18-8. Enartis describes potassium polyaspartate as a light brown powder.

Enartis describes the manufacturing process for potassium polyaspartate. Enartis states that L-aspartic acid is heated resulting in the formation of polysuccinimide. Then, polysuccinimide is reacted with potassium hydroxide under controlled conditions

¹ Part 6 of the notice received on March 20, 2018, contains material protected by copyright. FDA provided Enartis the option of rewriting Part 6 to address this issue and submitting it as an amendment.

² In the amended Part 6 of the notice, Enartis includes the 2016 European Food Safety Authority's conclusions³ based on unpublished toxicity studies that were subsequently published in 2017.

³ EFSA Panel on Food Additives and Nutrient Sources added to Food (2016).

allowing opening of the succinimide ring and polymerization of the units. The resulting 40% solution of potassium polyaspartate is spray dried to a powder form.

Enartis provides food grade specifications for potassium polyaspartate. These include an assay ($\geq 98.0\%$), limits on aspartic acid ($\leq 1.0\%$), potassium hydroxide ($\leq 2.0\%$), pH value (7.5–8.5 for 40% solution), and solubility in xylene, dichloromethane, methanol, acetone, ethyl acetate, and *n*-heptane (each $< 5.0 \text{ g/L}$). Enartis provides results of non-consecutive batch analyses to demonstrate that potassium polyaspartate can be manufactured to meet specifications.

Enartis summarizes an assessment of dietary exposures to potassium polyaspartate conducted by EFSA based on consumption data from several European countries.³ The population groups considered in the assessment included adults (18–64 years) and the elderly (≥ 65 years). Enartis reports that the mean dietary exposure to potassium polyaspartate at the maximum proposed use level is estimated to be 0.02–0.4 mg/kg body weight (bw)/day (d) for adults and 0.05–0.6 mg/kg bw/d for the elderly. At the high-level intake, the dietary exposure is estimated to be 0–1.4 mg/kg bw/d for adults and 0.4–1.8 mg/kg bw/d for the elderly. Enartis states that wine consumption in Europe is higher than in the U.S., and therefore considers that the EFSA dietary exposure estimates could be conservative.

Enartis discusses published data and information supporting the safety of consumption of potassium polyaspartate. The published *in vitro* digestibility study discussed by Enartis shows that less than 4% potassium polyaspartate is hydrolyzed following incubation with porcine pepsin and pancreatin. Enartis notes that based on the 4% breakdown of potassium polyaspartate, additional exposure to aspartic acid would be negligible (0.07 mg/kg bw/d at the intended maximum use level) compared to the estimated mean and high-level dietary exposure to aspartic acid (130 mg/kg bw/d and 186 mg/kg bw/d, respectively). The published oral toxicity studies in rats discussed by Enartis include a 14-day range-finding study and a 90-day oral toxicity study. The 90-day oral toxicity study shows that oral administration of up to 1000 mg/kg bw/d of potassium polyaspartate via gavage for 90 days did not produce any toxicologically relevant, treatment-related adverse effects. Enartis discusses the published bacterial reverse mutation assay, and the *in vitro* mammalian cell micronucleus assay, and concludes that potassium polyaspartate is neither mutagenic nor genotoxic. Enartis discusses an unpublished study that evaluated the interactions between potassium polyaspartate and minerals (using calcium, magnesium and iron as the representative minerals) and concludes that there is no significant mineral binding by potassium polyaspartate.

Based on the information presented in the notice, Enartis concludes that potassium polyaspartate is GRAS for its intended use in foods.

Section 301(l) of the Federal Food, Drug and Cosmetic Act (FD&C Act)

Section 301(l) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of

the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ii)(1)-(4) applies. In our evaluation of Enartis's notice concluding that potassium polyaspartate is GRAS under its intended conditions of use, we did not consider whether section 301(ii) or any of its exemptions apply to foods containing potassium polyaspartate. Accordingly, our response should not be construed to be a statement that foods containing potassium polyaspartate, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ii).

Conclusions

Based on the information that Enartis provided, as well as other information available to FDA, we have no questions at this time regarding Enartis' conclusion that potassium polyaspartate is GRAS under its intended conditions of use. This letter is not an affirmation that potassium polyaspartate is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 000770 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,
Michael A. Adams -S

Dennis M. Keefe, Ph.D.
Director
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

Digitally signed by
Michael A. Adams -S
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