

Summary of the dossier: D-allulose

Applicant: Samyang Corp., 295 Pangyo-ro, Bundang-gu, Seongnam-si, Gyeonggi-do, South Korea.

This submission concerns D-allulose manufactured by an enzymatic conversion of fructose to D-allulose using *Microbacterium foliorum* SYG27B-MF containing allulose-3-epimerase. *M. foliorum* SYG27B-MF, a non-genetically modified organism (non-GMO), was isolated from ginseng. D-Allulose, a naturally occurring monosaccharide, has 70% of the sweetness of sucrose and its energy value is estimated at 0.2 kcal/g. Allulose occurs in 2 forms: a crystalline form and a syrup form. It is produced by the epimerization of fructose at the C-3 position, in a reaction catalyzed by D-psicose 3-epimerase, which is contained within a non-viable, immobilized cell system, followed by standard purification processes in the edible carbohydrate industry (i.e., decolorization with activated carbon and purification by ion exchange and separation chromatography with intermittent concentration process). Purified allulose are concentrated (syrups) or crystallized (powder form only). Approval is sought for allulose, produced by non-GMO, as a Novel Food ingredient under Regulation (EU) 2015/2283.

Numerous human and animal studies have reported benefits of D-allulose with no major adverse effects. The following safety evaluation fully considers the composition, intake, and nutritional, microbiological, and toxicological properties of D-allulose as well as the appropriate corroborative data.

1. Analytical data from multiple lots indicate that Samyang's D-allulose complies reliably with the established food-grade product specifications, in particular the heavy metals and microbial purity, and meets all applicable purity standards.
2. Samyang Corp.'s D-allulose will be used as a sugar substitute in food applications at use levels ranging from 2 to 100% in selected foods as follows: bakery products (bakery products for diabetics); beverages (non-alcoholic; low- or reduced-calorie or sugar free); milk based beverages; breakfast cereals and cereals (regular, low- or reduced-calorie, sugar free); chewing gums; confections and frostings; frozen dairy desserts (ice cream, soft serve, sorbet; low- or reduced-calorie, sugar-free); yogurt (low- or reduced-calorie, sugar-free); dressings for salads; gelatins, pudding and fillings (low- or reduced-calorie, sugar-free); hard and soft candies ((low- or reduced-calorie, sugar-free); jams and jellies; sugar; sugar substitutes; sweet sauces and syrups (low- or reduced-calorie, sugar-free); and fat based cream.
3. Estimations of population mean intakes range from a minimum of 1.98 mg/kg bw/day in the very elderly to a maximum of 148.47 mg/kg bw/day in toddlers with 95% of studies having a mean intake under 96 mg/kg bw/day. Ninety-five per cent of studies have high level intakes under 213 mg/kg bw/day. Estimations of high level intakes range from a minimum of 0.90 g/day in infants and a maximum of 13.01 g/day in adults with 95% of studies having high level intake under 9.7 g/day. These exposure estimates are within safe intake levels of 0.5 to 0.6 g/kg bw/day or 31-33 g/person/day reported in the literature.
4. Since the specifications for the powder form of D-allulose in this submission are similar to those described for other sources of D-allulose, the metabolism, safety data and other pertinent information discussed for other sources of D-allulose (produced using various GMOs -CJ CheilJedang [US FDA, GRN 400], Matsutani Chemicals [US FDA, GRN 498], and Samyang Corp. [USFDA, GRN 693]) are applicable to the safety of Samyang's D-allulose in this novel food application. A subchronic toxicity study of D-

allulose reported that the NOEL was 5,000 mg/kg bw/day, the highest dose tested. Other sources of D-allulose also did not show adverse effects. A chronic toxicity study in rats showed that D-allulose (manufacturer- Matsutani Chemicals) at a dose of 1,280 mg/kg bw/day, the maximum level tested, did not show adverse effects. Due to substantial equivalence between Matsutani Chemicals' and Samyang's D-allulose in specifications (i.e., purity), the results found in the chronic toxicity study of another source of D-allulose can be applied when evaluating the safety of Samyang's D-allulose.

5. The LD50 value of D-allulose in rats is 15.8 -16.3 g/kg, indicating that D-allulose is an ordinary edible carbohydrate.

6. Safety of the non-GMO production microorganism, *Microbacterium foliorum*, has been fully proven through a battery of toxicity studies. *M. foliorum* was found to be not mutagenic or genotoxic. A 90-day subchronic toxicity in rats reported the NOEL value of 2,000 mg/kg bw/day, the highest dose tested, for the production organism, *M. foliorum* SYG27B-MF.

7. A human clinical study showed that the maximum tolerable levels in humans were 0.5 g/kg bw/day for males and 0.6 g/kg bw/day for females. The only side effect of non-digestible carbohydrates, including D-allulose, is gastrointestinal discomfort when ingested in large quantities (over 0.6-0.7 g/kg bw). This type of symptom is usually transient and is not considered of toxicological concern. Samyang's D-allulose at a daily dose of 12 g per day was well tolerated with no major side effects.

8. The proposed food use results in exposure levels below those associated with any adverse effects. The EDI assessments are based on the assumption that Samyang's D-allulose will replace currently marketed D-allulose. Thus, cumulative exposures are not expected. In addition, the EDIs presented in this notice are highly amplified estimates.

9. D-allulose has been safely used as a food ingredient around the world for a long time.

10. Since the inception of Samyang's D-allulose to the Korean market in March 2017, no adverse events were reported by consumers. Other sources of D-allulose has been marketed in USA, Mexico, Korea and Japan with no major side effects.

Overall, there are no indications of significant adverse effects related to D-allulose in the publicly available literature. Therefore, the proposed use of D-allulose is considered safe.