

**EPA position on the ANSES call for data on the use of nano-materials - Mannitol and Isomalt
do not fall under the definition of nano-engineered materials**

Background

In February 2019 the French Agence Nationale de Sécurité Sanitaire Alimentation, Environment Travail (ANSES) published a call for data on the use of nano materials in food, with focus on food additives and the aim to identify and list nano materials used in food.¹ Industry and other stakeholders have been invited to review that list, which inter alia included the polyols mannitol (E421) and isomalt (E 953). EPA membership provided ANSES within the deadline information and rationale to justify that both polyols do not fall under the definition of nano-engineered materials. The ANSES report² related to this call published in June 2020 included mannitol and isomalt among substances where the presence of nanomaterials is suspected but not confirmed.

Summary

Mannitol (E421) and Isomalt (E953) are polyols approved as food additives in the EU. They are produced with the use of traditional processes including gridding which can lead to unintentional creation of a very small number of particles with a size below 100 nm. However, polyols are also highly soluble which allows them to be placed on the market also in syrup forms. Based on available definition and characterization requirements, polyols are not considered as nanoengineered products but as conventional products. EPA believes this is in line with the current EFSA and other safety agencies interpretation.

Rationale

Mannitol and Isomalt are polyols authorized *quatum satis* as food additives in Europe in accordance with Regulation (EC) 1333/2008 on food additives.³ As other additives, the European Food Safety Authority (EFSA) is in charge of their safety assessment following strict rules laid down in Regulation (EC) 1331/2008.⁴ Currently, Mannitol and Isomalt as well as the other polyols, are being re-evaluated by EFSA⁵ according to Regulation (EU) 257/2010.⁶

EPA members perform on regular basis analyses of their products using different methods (see below) that allow to describe the particles size distribution and to determine the amount of particles above 100 nm. These methods are commonly used as granulometry is usually part of the specification of EPA members' powdered products.

For both, Isomalt and Mannitol, information on the particle size distribution was provided to EFSA as part of the dossier for their re-evaluation. Results have shown that more than 99% of the particles in both of these polyols are above 100 nm as analysed with (i) dynamic light scattering particle size analysis (solvent acetone) and (ii) laser diffraction analysis. This information has also been made

¹ https://www.anses.fr/fr/system/files/AppelContribution_Nanos.pdf

² <https://www.anses.fr/fr/content/nanomat%C3%A9riaux-dans-l%E2%80%99alimentation-les-recommandations-de-l%E2%80%99anses-pour-am%C3%A9liorer-leur>

³ <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32008R1333>

⁴ <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32008R1331>

⁵ <http://www.efsa.europa.eu/en/consultations/call/190513>

⁶ <https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32010R0257&from=EN>

available to ANSES (the French Agency for Food, Environmental and Occupational Health & Safety) in response to the ANSES call for data with regard to the use of nanoengineered materials in food.¹

EPA would like to stress that Isomalt and Mannitol are not in the scope of the definition of engineered nanomaterials provided for in Article 2(f) of Regulation (EU) 2015/2283 on Novel Foods.⁷

The European Commission⁸ has recommended a threshold of 50% of the particles in the number-based minimal external size distribution to be in the nanoscale (1–100 nm) for a material to be regarded as a nanomaterial. Although this level for nanomaterial definition is still under review, and has not yet been adopted under the relevant EU regulatory (food) frameworks, our results are showing levels much lower than this threshold.

In addition, the EFSA Guidance *on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health*⁹ is providing a structured pathway for carrying out safety assessment of nanomaterials in the food and feed area. With regard to this guidance document, polyols do not meet the criteria for nano-engineered materials:

1. All polyols are manufactured by standard technological processes which include crystallisation, crushing, milling, sifting and sieving which result in negligible amounts of particles smaller than 100 nm.
2. To our best knowledge and according to our literature search, nano-sized particles in polyols have no properties that are characteristic for the nanoscale (=different from the non-nano particles).
3. Data on water solubility are available based on suitable analytical techniques as requested in Annex C of the EFSA Guidance. According to chapter 4.3.3 of the guidance document, all polyols fulfil the criteria of “high solubility” as more than 1 mol/L is dissolved (Table 1).

Table 1. Data on solubility of polyols

Polyol	Commission regulation (EU) No 231/2012 as amended in 2017		Literature	
	Specification on Solubility	Method	Solubility in water	source
Mannitol (E 421)	soluble in water, very slightly soluble in ethanol, practically insoluble in ether	JECFA method	216 g/L (= 1.2 mol/L) at 25 °C	(1)
Isomalt (E 953)	Soluble in water, very slightly soluble in ethanol	Equivalent to JECFA method	1000 g/L (= 2.9 mol/L) at 25 °C	(2)

(1) <https://pubchem.ncbi.nlm.nih.gov/compound/6251#section=Solubility>

(2) <https://pubchem.ncbi.nlm.nih.gov/compound/88735#section=Solubility>

On the basis of the information provided above, EPA believes that the safety of Isomalt or Mannitol which contain very limited amount of nano-sized particles is sufficiently substantiated. The conclusion of the different agencies on the safety of Mannitol and Isomalt indeed concern these polyols including the negligible amount of particles below the size of 100 nm which may be unintentionally created by traditional processes such as crystallisation, crushing, milling, sifting and sieving.

⁷ Regulation (EU) 2015/2283 on novel foods:

https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=OJ:JOL_2015_327_R_0001

⁸ Commission Recommendation 2011/696/EU on the definition of nanomaterial;

<https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32011H0696>

⁹ <https://www.efsa.europa.eu/en/efsajournal/pub/5327>