



Comments to the Targeted Public Consultation for substance Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, hydrolysis products with silica; pyrogenic, synthetic amorphous, nano, surface treated silicon dioxide (CAS # 68909-20-6) (HMDZ-treated SAS).

6th of February, 2023

The Japan Inorganic Chemical Industry Association (JICIA) welcomes the opportunity to share its views and comment on the Targeted Public Consultation for substance HMDZ-treated synthetic amorphous silica (SAS). This consultation seeks comments on whether, based on the new acute inhalation toxicity study report (Fraunhofer ITEM Study No.02 G21 009), the current RAC opinion on the classification for acute inhalation toxicity of this substance as Acute Tox. 2; H330 should be revised.

Background:

In August 2021, the European Commission sent a technical notification to the WTO (G/TBT/N/EU/826) as regards to the draft amendment to the EU classification and labelling (CLP) Regulation (18th ATP), which includes a proposal to classify HMDZ-treated SAS as STOT RE 2; H373 (lungs, inhalation) and Acute Tox 2 via the inhalation route (H330). During the WTO consultation, JICIA communicated with the Ministry of Economy, Trade and Industry (METI), and commented as follows:

“JICIA kindly requests WTO and its members to raise and communicate their concerns to the EU Commission and ask it to reconsider the inhalation classification of HMDZ treated SAS, and to delay its adoption until all available studies have been properly addressed and evaluated.”

Following the submission of the study report and its review by JICIA, we would like to share the following important comment:

The points of new study in considering acute inhalation toxicity:

JICIA assessed the new study report (Fraunhofer ITEM Study) and the related paper (Frontier Public Health (2022)) ¹. JICIA considers the study to be very reliable as it was conducted in compliance with the regulations of the German Animal Protection Law, OECD Guideline No. 436 and the OECD Principles of Good Laboratory Practice. In both studies, a thorough histopathological examination of the entire respiratory tract, including different levels of the nasal cavities, larynx, trachea and lung was included



and an EDX analysis was performed to determine the chemical identity of agglomerated material. The study report clearly indicates that HMDZ-treated SAS is not toxic. The cause of death was demonstrated to be related to physical obstruction or “suffocation” of the upper respiratory tract, which is not an intrinsic hazard. According to the OECD-Guidance Document on inhalation toxicity studies Series on Testing and Assessment No. 39 (ENV/JM/MONO (2009) 28/REV1), paragraph 69 states “At very high concentrations, dry powder aerosols and chemically reactive liquid aerosols (e.g., polymers) tend to form conglomerates in the proximal nose causing physical obstruction of the animals’ airways (e.g., dust loading) and impaired respiration which may be misdiagnosed as a toxic effect.” **This OECD Guidance expressly points out that physical obstruction should not be misdiagnosed as a toxic effect.**

Conclusion:

Based on both studies, it is clear that the lethal effect in rats was initially caused by physical obstruction in the inhalation system, and not by the intrinsic toxicity of the substance tested. Clinical signs and findings in the lung were caused by such initial physical effects. As the OECD Guidance specifically warns that physical obstruction should not be misdiagnosed as a toxic effect, a classification as an acute toxicant of HMDZ-treated SAS is unwarranted. Consequently, **JICIA kindly requests that the current RAC opinion on the classification for acute inhalation toxicity of this substance as Acute Tox. 2; H330 be revised.**

About JICIA

Japan Inorganic Chemical Industry Association (JICIA) is a Japan based trade association, which was founded in 1948. Its head office is in Tokyo, and the branch office is in Osaka. There are 60 member companies with 19 product divisions, such as Amorphous silica division, Pigments division, Sodium silicate division and so on. JICIA deals with issues on safety, environment and health of the inorganic chemicals, working closely with ministries and related organizations.

Reference

1. Nils Krueger et al., “Physical Obstruction of Nasal Cavities With Subsequent Asphyxia, Causes Lethality of Rats in an Acute Inhalation Study With Hydrophobic HMDZ Surface-Treated Synthetic Amorphous Silica (SAS)”. *Frontiers in Public Health* June 2022, Volume 10, Article 907078.
(<https://www.frontiersin.org/articles/10.3389/fpubh.2022.907078/full>)