February 17, 2020

**WACKER comments on the targeted public consultation for harmonized classification and labelling on Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, hydrolysis products with silica (CAS 68909-20-6)**

It was surprising in two ways to see in an ECHA news alert the opinion of the RAC committee to classify hexamethyldisilazane surface-treated silica as Acute Tox 2.

First it had not been clear from the agenda of RAC that CAS 68909-20-6 would be discussed in the upcoming meeting. Putting “Silanamine” as a topic on the official agenda as surrogate for CAS 68909-20-6 was misleading and does not reflect the scientific standards claimed by the committee. “Silanamine” does neither represent a specific substance, nor does it indicate a modification of synthetic amorphous silica. It is acknowledged that the treatment agent of synthetic amorphous silica in the production of CAS 68909-20-6 is Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)- (i.e. hexamethyldisilazane, CAS 999-97-3). The substance Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)- is only used to describe CAS 68909-20-6 as a reaction product with synthetic amorphous silica. Chemically seen it is completely consumed and no “hazardous” amine function is transferred to CAS 68909-20-6 as the reader might conclude from “Silanamine”. The reaction product is a synthetic amorphous silica with methyl groups covalently bound to the particle surface. Although the RAC meetings are of no direct legislative relevance, such procedural flaws will render the CLH process for CAS 68909-20-6 a legally questionable and unfair process.

Secondly, it was surprising that studies from secondary literature (ECETOC 2006 and Becker at al. 2013) were used to conclude on a classification without a proper re-evaluation of the data. As a company owning some of the critical studies of synthetic amorphous silica treated with hexamethyldisilazane (see *Table 1*), we are aware that in ECEOC 2006 all studies were described as highly reliable according to a self-defined Code of Reliability. However, in the same report the data was further interpreted as not being relevant for defining the actual hazard of the product as used in the market. This view has not changed.

*Table 1 HDK® SKS acute inhalation toxicity studies as reported in ECTOC 2006. The surface of these synthetic amorphous silica grades is modified by 1,1,1,3,3,3-Hexamethyldisilazane*

| Product name | MMAD [µm] | GSD | Type of exposure | Doses tested [mg/m³] |
|---|---|---|---|---|
| HDK® SKS 130 | <0,2 | 4.78-9.71 | whole body | 350, 770, 2530, 5300 |
| HDK® SKS 130 | 7,7-7,7 | 3.24-4.25 | nose only | 900, 2200 |
| HDK® SKS 300 | <0,1 | n.a. | whole body | 90, 350, 5000 |
| HDK® SKS 300 | 7-7,1 | 4.2-5.2 | nose only | 400, 600 |
| HDK® SKS 300 VI | <0,4 | 5.4 – 15.1 | whole body | 80, 340, 1200, 5000 |
| HDK® SKS 300 VI | 6,3-7,7 | 5.5 | nose only | 400, 700, 2000 |

Due to the registration requirements for nanoforms under REACH beginning 2020 all data on surface treated silica had to be reassessed according to the Klimisch code. According to the reliability scoring by Klimisch et al. a study should be assigned to category 3 (not reliable) if one of the following points apply:

- there are interferences between the measuring system and the test substance
- organisms/test systems were used which are not relevant in relation to the exposure
- carried out or generated according to a method which is not acceptable

In the studies in *Table 1* huge efforts were made to achieve the acute inhalation toxicity limit concentration for dust of 5 mg/L under the requirements of the OECD 403 test guideline. Whole body exposure vs. nose only exposure, different particle dispenser and resizer to break down agglomerates as well as target concentration up to 21 mg/L in the chamber were only some of the variables changed to achieve this goal. However, all these efforts to increase the high dose concentration led to a huge particle load in the deeper rat lung at all tested concentrations with a deposition characteristic that cannot be judged as relevant in relation to the known particle exposure of the substance as used in the market. Resizing spherical particles by breaking agglomerates cannot be considered as a simple adaption of the particles dimension to the rat respiratory tract dimension. Properties like material density, reagglomeration tendency and wetting behavior are important drivers of physical behavior of the particle in the lung and consequently the local particle load. In most experiments in *Table 1,* a very low particle size far below the recommendations of the OECD guidance were observed. However, in the experiments conducted with a higher MMAD above 5 µm, an observed GSD of >4 indicates that there is still a large fraction of small particles present in the air which were formed during generation of the test atmosphere. Reaching the tiny respiratory tract structures of the laboratory animals with small sized but still bulky spherical and hydrophobic particles probably caused fatal local blockage but has little to do with a realistic exposure situation of humans. Consequently, we concluded that all studies in *Table 1* must be categorized as Klimisch 3 (test system is not relevant in relation to known exposure) and therefore cannot be used for the assessment of the endpoint acute inhalation toxicity.

Mechanistic studies as proposed by external experts (Dekant and Bosch, 2020) are already contracted by the REACH consortium and will focus on suffocation as the proposed mode of action. Suffocation would be a non-specific severe disturbance of the OECD 403 test system designed to identify specific systemic effects or interactions with the physiology of the lung. Identifying suffocation as mode of action would question the applicability of the standard acute inhalation toxicity methods for particles like SAS.

As soon as the results of the mechanistic studies are obtained, an update of the REACH dossier will reflect all available information on acute inhalation toxicity of synthetic amorphous silica (surface-modified and non-modified form), with an adequate scientific interpretation for classification and labelling.

Literature:

ECETOC (2006). Synthetic Amorphous Silica (CAS No. 7631-86-9). JACC Report no. 51, September 2006, European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC), Brussels

Becker et al. (2013). Safety assessment of silylates and surface-syloxysilicates, International Journal of Toxicology 32(Supplement 1) 5S-24S

Dekant and Bosch (2020). Review of acute inhalation studies on SAS and surface-modified SAS to generate an expert statement on classification and labeling needs.