Agency technical report on the classification and labelling of:

Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1] Silica gel, pptd., cryst.-free; Precipitated silica, silica gel, colloidal silica, amorphous, nano [2]

EC Number: - [1]; - [2]
CAS Number: 112945-52-5 [1]; 112926-00-8 [2]

April 2026

Contents

Brief summary

The conclusion of the Agency technical report for Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1]; Silica gel, pptd., cryst.-free; Precipitated silica, silica gel, colloidal silica, amorphous, nano [2] is:

STOT RE: no classification proposed – further assessment needed.

Is this in agreement with the RAC opinion? **NO**

The RAC Opinion proposed classification as STOT RE 1; H372 (Causes damage to the respiratory tract through prolonged or repeated exposure via inhalation). The Agency is aware that extra scientific information not discussed in the RAC opinion is available. Therefore, to conduct a full assessment of all available data, synthetic amorphous silica will be assessed for STOT RE in a targeted Article 37A MCL proposal.

At the time of publication, this mandatory classification and labelling (MCL) has not been agreed and/or adopted in Great Britain.

This is a targeted technical report which only considers Specific Target Organ Toxicity (STOT RE). This was the only hazard class considered in the EU Committee for Risk Assessment (RAC) Opinion.

Introduction

Under Article 37 of the GB CLP Regulation[1], the Agency[2] is required to produce a technical report for each substance on which the Committee for Risk Assessment (RAC) of the European Chemicals Agency produces an opinion3.

This technical report documents an independent scientific assessment, conducted by HSE technical specialists of the classification and labelling of Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1]; Silica gel, pptd., cryst.-free; Precipitated silica, silica gel, colloidal silica, amorphous, nano [2].

Table 1. Information considered in the scientific assessment

Document	**Included in assessment**
EU CLH report	Yes
Annexes to the EU CLH report	Yes
RAC opinion	Yes
Background document	Yes
Information submitted during the EU public consultation process (RCOM table, including attachments)	Yes
RAC minority opinion(s)	Not applicable
Other information:	No

This information has been evaluated against the classification and labelling criteria set out in the GB CLP Regulation.

[1]The retained CLP Regulation (EU) No. 1272/2008 as amended for Great Britain

[2] HSE acting in its capacity as the GB CLP Agency

[3] Under Article 37(4) of Regulation (EU) No 1272/2008 on classification, labelling and packaging of substances and mixtures

Overview of current and proposed classification and labelling

Table 2. Current and proposed classification and labelling

	Index No.	International Chemical Identification	EC No.	CAS No.	Classification		Labelling			Specific Concentration Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard Statement Code(s)	Pictogram, Signal Word Code(s)	Hazard Statement Code(s)	Suppl. Hazard Statement Code(s)		
GB MCL List entry	N/A	No current entry									
EU dossier submitter's proposal	TBD	Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1] Silica gel, pptd., cryst.-free; Precipitated silica, silica gel, colloidal silica, amorphous, nano [2]	-[1] -[2]	112945-52-5 [1] 112926-00-8 [2]	STOT RE 1	H372 (respiratory tract) (inhalation)	GHS08 Dgr	H372 (respiratory tract) (inhalation)			
EU RAC opinion	TBD	Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1] Silica gel, pptd., cryst.-free; Precipitated silica, silica	-[1] -[2]	112945-52-5 [1] 112926-00-8 [2]	STOT RE 1	H372 (respiratory tract) (inhalation)	GHS08 Dgr	H372 (respiratory tract) (inhalation)			

	Index No.	International Chemical Identification	EC No.	CAS No.	Classification		Labelling			Specific Concentration Limits, M-factors	Notes
					Hazard Class and Category Code(s)	Hazard Statement Code(s)	Pictogram, Signal Word Code(s)	Hazard Statement Code(s)	Suppl. Hazard Statement Code(s)		
		gel, colloidal silica, amorphous, nano [2]									
Agency technical report conclusion	N/A	No MCL list entry									
Resulting MCL entry on GB MCL list	N/A	No MCL list entry									

N/A: not applicable

TBD: to be determined

Background

Active substance in Plant Protection Products: ☐

Active substance in Biocidal Products: ☒

Chemical registered under REACH: ☒

This technical report and corresponding RAC opinion (ECHA, 2025) covers **synthetic amorphous silica, without surface modification**. An EU harmonised classification and labelling (CLH) proposal was submitted in 2023 to address a concern for repeated dose toxicity via the inhalation route, with the dossier submitter (DS) noting that this hazard had not been reflected in self-classifications submitted by notifiers in the EU (CLH, 2023).

Synthetic amorphous silica (SAS) is a type of silicon dioxide (CAS 7631-86-9). Other types of silicon dioxide also covered by this CAS number were excluded from the scope of the RAC opinion, owing to differences in their structure and composition compared with SAS; these include crystalline silica (e.g., quartz), natural amorphous silica (e.g., kieselguhr) and silica by-products (e.g., silica fume) (CLH, 2025).

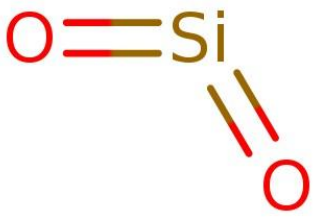

Figure 1: structural formula of silicon dioxide (taken from ECHA CHEM[4])

SAS may be modified at the surface, for instance with silanes or siloxanes, to result in differences in reactivity and toxicological properties. Therefore, SAS with surface modifications were also excluded from the assessment (CLH, 2023). One SAS with surface modification, silanamine, has previously been assessed by RAC and the Agency under EU and GB CLP, respectively (ECHA, 2019; HSE, 2021; HSE, 2025). Silanamine currently has a GB MCL of STOT RE 2; H373 (lungs, inhalation).

[4] https://chem.echa.europa.eu/

For the purposes of this assessment, the term SAS is used to refer to synthetic amorphous silica without surface modifications and without specification of type. The RAC opinion identified four different types of SAS: pyrogenic/fumed silica, which is produced via a thermal production process, and precipitated silica, silica gel and colloidal silica, which are all produced via wet production processes (ECHA, 2025). RAC included both nano and non-nanoforms of SAS within the scope of their assessment. A summary of the physicochemical properties of the four different types of SAS identified by RAC is provided in Table 3.

Table 3: compilation of the physical and chemical properties of different SAS types (ECETOC, 2006; Fruijtier-Pölloth, 2012; OECD SIDS, 2004), taken from page 3 of the RAC opinion (ECHA, 2025)

Property (units)	Pyrogenic	Precipitated	Colloidal	Gel
SiO_2 content (% ww)	≥ 99.8	> 95	≥ 99.5	> 95 (dry)
Loss on drying (%)	< 2.5	5-7	50-85	2-6
Density (g/cm^3)	2.2	1.9-2.2	1.9-2.2	1.8-2.2
Water solubility (saturation), (mg/L) at 37°C and pH 7.1-7.4	144-151	141	Colloidal dispersion in water	127-141
pH (1:1 water:ethanol)	3.6-4.5	5-9	3.5-4.4 (4% w/v aqueous dispersion)	3-8
Specific surface area, B.E.T. (m^2/g)	50-500	30-800	50-380	250-1000
Primary particle size (nm)	5-50	5-100	1-10	1-10
Aggregate size in bulk (µm)	0.1-1	0.1-1	0.1-1	1-20
Agglomerate size in bulk (µm)	1-250	1-250	1-250	1-250

Additionally, the hazard evaluation in the CLH report and RAC opinion only covered inhalation exposure to SAS in the form of dusts, mists and fumes. Non-inhalable liquid dispersions, such as silica gel and colloidal silica, were excluded from the assessment. The DS proposed to address this with the addition of a note ('*This classification applies only to mixtures that may lead to exposure of the end-user's lungs by inhalation'*); however, RAC considered that liquid preparations of SAS would automatically be excluded from the requirement to classify based on the specification of exposure route (inhalation) in the Annex VI entry, and therefore the addition of a note was not necessary.

Toxicokinetics

Toxicokinetic data were available with pyrogenic and precipitated silica, but were limited to measurements of the deposition of particles in the lungs and mediastinal lymph nodes after inhalation exposure of rats and guinea pigs (CLH, 2023). Si and SiO_2 particles were identified in both organs after inhalation. Clearance rates varied, with some studies identifying the presence of particles in lungs and lymph nodes at observations taken as long as 3 months after exposure (CLH, 2023).

Scientific assessment of the physical, human health and environmental hazard classes

Physical Hazards

Not assessed in the CLH report or RAC opinion.

Health Hazards

Acute Toxicity

Not assessed in the CLH report or RAC opinion.

Specific target organ toxicity – single exposure (STOT SE)

Not assessed in the CLH report or RAC opinion.

Skin corrosion/irritation

Not assessed in the CLH report or RAC opinion.

Serious eye damage/irritation

Not assessed in the CLH report or RAC opinion.

Respiratory sensitisation

Not assessed in the CLH report or RAC opinion.

Skin sensitisation

Not assessed in the CLH report or RAC opinion.

Specific target organ toxicity – repeated exposure (STOT RE)

Classification agreed by RAC:

Human and animal data were available to assess STOT RE. The assessment focused on inhalation toxicity after exposure to different types of SAS; a summary of the different types of SAS discussed in this section is given in table 4.

Table 4: Comparative table of SAS types and forms discussed under STOT RE (adapted from page 13 of the CLH report; CLH, 2023)

Name	Type	Specific surface area (BET) [m2/g]	Purity
AEROSIL OX50	Pyrogenic	40-50	> 99.8%
Cab-O-Sil	Pyrogenic	400	> 99.8%
AEROSIL 200	Pyrogenic	200	> 99.8%
Cab-O-Sil M5	Pyrogenic	200	> 99.7%
VA-Kieselsäure LGS	Pyrogenic	-	-
SIPERNAT 22S	Precipitated	190	98%
NM-200	Precipitated	190-220	
Kieselsäure FK 700/ SIPERNAT 700	Precipitated	700	
SYLOID 74	Silica gel	200	> 99.5%
LUDOX	Colloidal	130	Colloidal silica particle dispersed in water
SiO2 naked	Colloidal	-	-

Human data

Six epidemiological studies were available, assessing the effects of occupational inhalation exposure to SAS.

Morfeld *et al*. (2014) and Taeger *et al*. (2016) described a cross-sectional study in 484 male workers across five German SAS production plants. All participants were full-time employees, and the duration of employment ranged from 0.1-14.8 years (median: 12.4 years). The effects of cumulative exposure to inhalable SAS (pyrogenic and precipitated) were evaluated using symptoms, spirometry and chest films. Two exposure scenarios were determined, the first using expert assessment only and the second using expert assessment and personal SAS measurement data. Average cumulative exposure estimates based on all 484 workers were 31.8 mg/m^3·years (with a range of 0.1-419) based on the expert assessment-only scenario, and 56.9 mg/m^3·years (with a range of 0.4-480) based on the expert assessment + personal measurement scenario. Of all participants, 11% were found to have chronic bronchitis, although the DS noted that the relationship between this effect and exposure was not consistent across the two exposure scenarios. Chest films did not reveal any incidences of pneumoconiosis. Forced vital capacity (FVC) was reduced in one exposure scenario, but there were no effects on forced expiratory volume in 1 second (FEV_1) or FEV_1/FVC. An extended analysis of the data did not reveal any adverse effects on FEV_1 or FEV_1/FVC after exposure to respirable SAS dust, but did indicate a reduction in FVC.

A second cross-sectional study was also available, conducted in workers at a chemical plant engaged in the synthesis of amino acids and vitamins (Choudat *et al*., 1990). A group of 41 workers exposed to precipitated SAS via inhalation were compared with an unexposed control group of 90 workers from the same plant, and effects evaluated using chest X-rays, pulmonary function and blood gas analysis. The control and exposed groups had similar percentages of smokers (46% in the exposed group and 42% in the control). No effects of SAS inhalation were identified using chest X-rays or blood gas analysis in the exposed group. However, there were decreases in lung function parameters, in the form of reduced FEV_1/FVC and mean forced expiratory flow (FEF) values (FEF_{25-75}, FEF_{50} and FEF_{75}). All three mean FEF values were reduced in smokers and exposed workers compared to non-exposed smokers, with the DS noting that the difference was only significant between smoking-exposed and non-smoking non-exposed groups.

A cohort study was also available, conducted in 40 workers at a metallurgical company, who were exposed to pyrogenic SAS via inhalation (Vitums *et al*., 1977). SAS dust particle size ranged from 0.05-0.75 µm. The duration of employment ranged from 11-18 years. X-ray analysis of all participants revealed lung abnormalities in 11/40 workers. Three of these workers (all smokers) were selected for further investigations via spirometry and biopsy. In this group, Worker 1 and Worker 3 showed moderate-severe reductions in FEV_1 along with mild-moderate reductions in diffusing capacity for carbon monoxide. Biopsies of

Worker 1 and Worker 2 showed subpleural peribronchial and perivascular fibrosis, pigment in connective tissues, intraalveolar macrophages and emphysema, with milder effects in Worker 2 than Worker 1. According to the DS, a review conducted by a pathology institute identified similarities between the observed fibrohystiocytic nodules and descriptions of pneumoconiosis caused by amorphous silica in other studies.

The final three epidemiological studies were assessments of health and medical records of workers exposed to SAS. Plukett and DeWitt (1962) assessed the company health records of 78 male workers involved in the production of precipitated silica (Hi-Sil) and hydrated calcium silicate (Silene) in the USA. Duration of employment ranged from 1 year to 16 years and 7 months (mean = 4.75 years), with the percentage of time each worker was exposed to SAS ranging from < 30% (7/78), to 50-90% (31/78), to 100% (40/78). SAS levels ranged from 0.3-204 mg SiO_2/m^3. Health records consisted of yearly X-rays and self-reporting of symptoms; these symptoms included irritation of exposed skin, eyes, nose and throat from contact with dry dust, and thermal burns of skin and eyes from wet slurry. However, there were no differences in the incidence or type of injury reported across different groups of workers. Additionally, yearly X-rays did not indicate any cases of silicosis or pulmonary diseases.

Volk (1960) evaluated chest X-rays from 215 workers involved in the production of pyrogenic SAS (AEROSIL) in Germany. The average duration of exposure was not calculated, but the DS noted that only 9/215 participants had been employed for over 10 years. X-ray data was collected from 1947-1959. Airborne SAS measurements were only taken at the end of this period, in 1959, with levels ranging from 2-7 mg SiO_2/m^3 in the bagging and production rooms, and reaching 15-100 mg SiO_2/m^3 at the filling nozzle, although it was not clear whether the higher exposure levels at the filling nozzle would have been within the breathing zone of the workers. X-rays did not identify silicosis in any of the workers in this study.

Lastly, an assessment of medical records of 165 workers involved in the manufacturing of precipitated SAS (Hi-Sil and Silene) across two industrial facilities in the USA was available (Wilson *et al*., 1979). All participants were exposed to SAS for at least 1 year, with exposure duration ranging up to 35 years with a mean of 8.6 years. The assessment consisted of a review of all spirograms, respiratory questionnaires and chest radiographs. Linear regression did not reveal any correlation between exposure to SAS (dose or time) and changes in pulmonary function. Chest radiography identified 11/165 workers with pneumoconiosis, but all 11 had also been previously exposed to limestone mines or soda ash plants using limestone, which contained crystalline silica. Of the 165 workers, 143 were confirmed to have only been exposed to SAS and were subject to serial radiographs; none of these 143 workers showed pneumoconiosis.

Of the available epidemiological studies, RAC concluded that the three assessments of medical/health records did not show any effects after occupational exposure to SAS

(Plukett and DeWitt, 1962; Volk, 1960; Wilson *et al*., 1979). They concluded that the cross-sectional study by Choudat *et al.* (1990) and the cohort study by Vitums *et al.* (1977) found some evidence of effects (e.g., reductions in lung function parameters in the cross-sectional study and lung abnormalities in the cohort study); however, the effects of SAS inhalation could not be separated from the confounding factor of smoking habits of participants in either study. Lastly, RAC concluded that no consistent exposure-effect relationship could be identified in the first cross-sectional study (Morfeld *et al*., 2014; Taeger *et al*., 2016; Yong *et al*., 2022).

Comments received during the public consultation suggested that the lack of positive associations between SAS exposure and pulmonary effects in the human epidemiological data should be taken into account in the conclusion on classification, based on the STOT RE classification criteria, which state that a conclusion may be drawn based on '*reliable and good quality evidence from human cases or epidemiological studies*' (CLP Annex I, Table 3.9.1).

RAC conclusion on human data

RAC concluded that there was no conclusive evidence that SAS caused fibrogenic effects in the lungs of humans. However, they noted that adequate assessment of bronchitis, airway obstruction and emphysema after chronic exposure to SAS was lacking in the available dataset. Additionally, they considered the human data to suffer from limitations relating to confounding factors such as smoking, the potentially long progression of effects, and incomplete assessment of exposure levels. RAC considered a further limitation of the data to be the inclusion of only workers still in employment, which they suggested could have led to underestimation of the effects of SAS exposure via a healthy worker survivor effect (HWSE).

The largest epidemiological study was the cross-sectional study by Morfeld *et al*. (2014), with 484 participants. As described above, RAC concluded that there was no consistent exposure-effect relationship in this study. However, they noted that the study authors themselves considered the two exposure scenario approaches used to '*suffer from considerable uncertainties that need to be considered in epidemiological studies'*. Although no positive result was obtained in this study, RAC considered that solid evidence of a positive or negative association should be based on a '*very thorough epidemiological study with a large(r) study population*' (ECHA, 2025), and therefore concluded that the study by Morfeld *et al*. was not powerful enough to prove that toxicity would not occur in humans.

RAC further noted that SiO_2 dust concentration levels in the workplace have reportedly reduced by two orders of magnitude since the beginning of mass production of AEROSIL pyrogenic SAS in 1959, and therefore considered it possible that potential toxic exposures to SAS in factory workers have been minimised by existing control measures. Despite this,

they acknowledged that there are some reports of lung effects in workers after chronic SAS exposure, including the cross-sectional study by Choudat *et al.* (1990) and the cohort study by Vitums *et al.* (1977).

Overall, RAC concluded that the human data could not be considered 'reliable and good quality evidence' as required by Annex I, Table 3.9.1 of the CLP Regulation. They further referred to Annex I, Section 3.9.2.7.2 of the CLP Regulation, which states that '*Evidence from human experience/incidents is usually restricted to reports of adverse health consequence, often with uncertainty about exposure conditions, and may not provide the scientific detail that can be obtained from well conducted studies in experimental animals*'. Based on this, RAC concluded that the available human epidemiological data were not sufficient to draw a conclusion on classification according to the CLP classification criteria.

Animal data

A large number of repeated dose studies were available with pyrogenic silica, precipitated silica, silica gel and colloidal silica. Both the DS and RAC considered the most relevant studies to be those of sufficient quality, with exposure times of at least 28 days, multiple doses and at least 10 animals/sex/dose. A summary of the available information is provided in Table 5.

Table 5: Summary table of repeated dose toxicity animal studies, with those considered most relevant for RAC's assessment highlighted in red. Adapted from pages 14-19 of the CLH report (CLH, 2023)

Study details	Results	Reference
Studies with pyrogenic silica		
OECD TG 413 **GLP** Male and female Wistar rats (Crl:WI (Han)) 10/10 exp + 1d 5/5 exp + 90/180/360d Exposure: 90-d 6h/d, 5d/wk Recovery periods: 0, 90, 10, 360d Nose-only inhalation: 0.5, 1, 2.5 and 5 mg/m^3 (nominal) Test substance:	Effects of both SAS substances included interstitial inflammation, granuloma, fibrogenesis and fibrosis of the lungs and lymph nodes. There was a link between surface area and severity/persistence of effects; higher incidence, severity and duration was associated with low BET particles. LOAEC SAS 1: 1 mg/m^3 LOAEC SAS 2: 0.5 mg/m^3	Fraunhofer ITEM, 2019

Study details	Results	Reference
AEROSIL: Cab-O-Sil (SAS1; high surface area) and OX50 (SAS2; low surface area) Mean MMAD: 2.08-3.04 µm (SAS1); 1.30-2.20 µm (SAS2) Mean GSD: 2.16-3.53 (SAS1); 2.90-3.53 (SAS2)	Further discussion of effects in the text below.	
Comparable to OECD TG 413 GLP Male and female Wistar rats (Cpb: WU Wistar random) 20/20 exp 10/10 exp + 13/26/39 wks 20/20 exp + 52 wks Exposure: 13 wks 6h/d, 5d/wk Recovery periods: 0, 13, 26, 39, 52 wks Inhalation (whole-body): 1, 6, 30 mg/m^3 (nominal) Test substance: AEROSIL 200 MMAD not determined	Dose dependent increases in accumulation of alveolar macrophages, cellular debris, intra-alveolar polymorphonuclear leucocytic infiltration, increased septal cellularity, alveolar bronchiolization, focal interstitial fibrosis, cholesterol clefts. Fibrosis incidence increased with increasing duration of the recovery period LOAEC (all effects): 1 mg/m^3 LOAEC (fibrosis): 30 mg/m^3 Re-evaluation of slides from 10 males/dose according to a newer scoring system did not detect fibrosis, but did detect macrophage aggregations and granulomas (reversible within 13-52 wks). Further discussion of effects in text below.	Reuzel *et al*., 1991 and Weber *et al*., 2018
OECD TG 413 Fischer 344 rats (4 males/time point) Focused on pulmonary effects in comparison with crystalline silica Test substance: AEROSIL 200 MMAD (µm): 0.81	Reversible changes in all bronchoalveolar lavage (BAL) parameters. Elevated numbers of neutrophils and macrophages and some fibrosis in the alveolar septa of lungs. LOAEC: 50.4 mg/m³ air (analytical)	Johnston *et al*., 2000

Study details	Results	Reference
Exposure: 50.4 mg/m³ air (analytical) Whole body inhalation 13 wks 6h/d, 5d/wk Recovery 0, 12 and 32 wks		
Non-guideline SD rats, guinea pigs, and Cynomolgus monkeys (80 rats, 20 guinea pigs, 10 monkeys per group) Exposure: 18 months 5.5-6h/d, 5d/wk No recovery period Inhalation (whole body): 15 mg/m^3 Some monkeys unintentionally exposed to mica and kaolin as well as the test substance; not reported to have affected the results Test substance: Pyrogenic silica (not further specified) Geometric mean: 0.17 µm	Strongest effects were seen in monkeys. There was deposition of large quantities of amorphous silica in macrophages in the lungs and tracheal lymph nodes of monkeys. Early nodular fibrosis was seen in the lungs of 6 out of 9 exposed monkeys. Also pulmonary function parameters were significantly different.	Groth *et al.*, 1981
OECD TG 412 (adapted as 5-day study) **GLP** Wistar albino rats (10 males/dose/time point) Exposure: 5-d 6h/d Recovery periods: 0, 4, 13 wks Inhalation (nose-only): 1, 5, 25 mg/m³ (nominal)	Increased lung weight and increase in inflammatory markers at mid and high dose. Changes were reversible after 3 months. LOAEC: 5 mg/m^3	Anonymous, 2003a Published by Arts *et al.*, 2007

Study details	Results	Reference
Test substance: Cab-O-Sil M5 MMAD (µm): 1.70-1.94 GSD: 1.70-1.79		
OECD TG 412 (adapted as 5-day study) **GLP** Wistar rats (10 males/dose/time point) Exposure: 5-d 6h/d Recovery periods: 0, 4, 13 wks Inhalation (nose-only): 1, 5, 25 mg/m³ (nominal) Test substance: VA-Kieselsäure LGS/VA-silica LGS MMAD (µm): 1.57-2.07 GSD: 2.10-2.34	At the high dose intraepithelial and peribronchial infiltration of polymorphonuclear inflammatory cells, accompanied by slight hypertrophy and/or hyperplasia of the bronchiolar epithelium. LOAEC: 25 mg/m^3	Anonymous, 2009
Studies with precipitated silica, silica gel or colloidal silica		
Comparable to OECD TG 413 **GLP** Male and female Wistar rats (Cpb: WU Wistar random) 20/20 exp 10/10 exp + 13/26/39 wk recovery 20/20 exp + 52 wk recovery Exposure: 13wks 6 h/d Inhalation (whole body): 30 mg/m^3	Accumulation of alveolar macrophages in the lung, reversible after 39 weeks	Reuzel *et al.*, 1991

Study details	Results	Reference
Test substance: SIPERNAT 22S MMAD not determined		
OECD TG 413 Male Wistar rats 55/dose Exposure: 13 wks 6h/d, 5d/wk Recovery periods: 0, 90d Inhalation (nose-only): 1, 2.5, 5 mg/m^3 (nominal) Test substance: NM-200 MMAD: – low dose: 2.16 µm, GSD: 0.09 – mid dose: 2.94 µm, GSD: 0.2 – high dose: 3.12 µm, GSD: 0.06	Increased lung weights (mid and high dose), persistent inflammatory responses in the nasal cavity in all dose groups and transient inflammatory effects in the lungs in mid and high dose groups.	Anonymous, 2014a Reviewed by Creutzenberg *et al.*, 2022
Non-guideline SD rats, guinea pigs and Cynomolgus monkeys 80 rats/20 guinea pigs/10 monkeys/group Exposure: 18 months 5.5-6 h/d, 5 d/wk No recovery period Inhalation (whole body): 15 mg/m^3 Test substance: Silica gel and precipitated silica (not further specified)	Strongest effects were seen in monkeys. There was deposition of large quantities of amorphous silica in macrophages in the lungs and tracheal lymph nodes of exposed monkeys. Monkeys exposed to precipitated silica demonstrated significantly lower lung volumes compared with controls, while monkeys exposed to silica gel had significant changes in ventilatory performance and mechanical properties	Groth et al., 1981

Study details	Results	Reference
MMAD (µm): 0.27 (gel), 0.38 (precipitated)		
Non-guideline, very limited reporting Rats (110 females) Exposure: 1 year 6 h/d, 5 d/wk 5 month recovery period (16 rats) Inhalation (whole body): 55 mg/m^3 (analytical) Test substance: Kieselsäure FK 700 (SIPERNAT 700) MMAD unknown	Some bronchial effects were shown after 1 year of exposure, but they mostly subsided after 5 months of recovery. No fibrosis was detected.	Klosterkotter, 1968b
Short term rep dose study Crj: CD (SD) rats 25 males/dose 10 exp 5 exp + 10d recovery 10 exp + 3m recovery Exposure: Inhalation (whole body): 10, 50, 150 mg/m^3 4 wks Test substance: LUDOX CL-X MMAD (µm): 2.9-3.7 GSD: 1.9-2.3	At mid and high dose reversible increase in lung weights, alveolar macrophage response, polymorphonuclear leukocytic infiltration, and Type II pneumocyte hyperplasia in alveolar duct regions.	Anonymous, 1990 Lee and Kelly, 1992 Warheit, 1991
OECD TG 412 Wistar rats 35 males/dose Exposure:	Slight to moderate mucous (goblet) cell hyperplasia (5 of 5 males of the high-dose group) and dose dependent epithelial eosinophilic droplets in the nasal cavity; in the high dose group, the epithelial eosinophilic droplets were associated with	Anonymous, 2014b

Study details	Results	Reference
14-d 6 h/d, 5 d/wk 14-d recovery Inhalation (nose-only): 1, 5, 25 mg/m^3 (nominal) Test substance: NM-200 MMAD: – low dose: 0.69 µm, GSD: 6.95 – mid dose: 2.87 µm, GSD: 1.97 – high dose: 3.16 µm, GSD: 1.7	(multi)focal subepithelial inflammatory cell infiltration. A significant increase of alveolar/interstitial macrophage infiltration and of (multi)focal very slight alveolar granulocyte infiltration in the lungs of the high dose group. Multifocal 'granuloma like' foci of macrophages (histiocytosis) in the lung associated lymph nodes of 3/5 high dose rats	
Range-finding study Wistar rats 5 males/dose Exposure: 5-d Inhalation (nose-only): 1, 5, 25 mg/m^3 (nominal) Test substance: NM-200 MMAD: – low dose: 2.12 µm, GSD: 3.15 – mid dose: 3.47 µm, GSD: 2.31 – high dose: 2.29 µm, GSD: 3.44	Dose-dependent mucous cell hyperplasia in the respiratory epithelial lining of the nasal septum and nasal meatus, very slight bronchiolo-alveolar hyperplasia and very slight to slight bronchial mucous cell hyperplasia in the lungs at the top dose.	Anonymous, 2014c
OECD TG 412 (adapted as 5-d study) Wistar albino rats 10/males/dose/time point	The high dose induced changes in differential cell count and biochemical parameters in BAL fluid, increased weights of lungs and tracheobronchial lymph nodes, and histopathological changes, reversible after one month except a light increase in	Anonymous, 2003b Published by Arts et al., 2007

Study details	Results	Reference
Exposure: 5d 6h/d 4 and 13 wk recovery Inhalation (nose-only): 1, 5, 25 mg/m^3 (nominal) Test substance: SYLOID 74 MMAD (µm): 1.57-1.71 GSD: 1.51-1.60	lung collagen content after three months. At the mid dose, there was a slight but significant increase in the percentage of neutrophils in BAL fluid.	
OECD TG 412 (adapted as a 5-d study) Wistar albino rats 10 males/dose/time point Exposure: 5-d 6 h/d 4 and 13 wk recovery Inhalation (nose-only): 1, 5, 15 mg/m^3 (nominal) Test substance: ZEOSIL 45 MMAD (µm): 2.83-3.27 GSD: 1.75-1.90	The high dose induced changes in differential cell count and biochemical parameters in BAL fluid, increased weights of lungs and tracheobronchial lymph nodes, and histopathological changes, reversible after one month. At the mid dose there was a slight increase in relative neutrophil count in BAL fluid.	Anonymous, 2003c Published by Arts et al., 2007
Short term inhalation study (according to protocol by NanoSafe2) Han Wistar rats 5 males/dose Exposure: 5d 6 h/d 3 wk recovery	Multifocal macrophage aggregates were observed in the lung shortly after exposure. This finding exacerbated towards a slight multifocal pulmonary inflammation by the end of the 3-week exposure free period.	Landsiedel et al., 2014

Study details	Results	Reference
Inhalation: 0.5, 2.5, 10, 50 mg/m^3 Test substance: Colloidal uncoated amorphous silica (SiO_2 naked) MMAD (µm): 1.0-2.2 GSD: 2.2-3.4		

RAC identified four key studies: Fraunhofer ITEM (2019), Reuzel *et al.* (1991), Creutzenberg *et al*. (2022) and Anonymous (1990; discussed by Lee and Kelly (1992) and Warheit (1991)). The first of these was a 90-day repeated dose study conducted according to OECD TG 413 (Fraunhofer ITEM (2019)). Wistar rats (10/sex/group) were exposed to two types of Aerosil (pyrogenic silica) via nose-only inhalation for 90 days (6 h/d, 6 hr/wk) and sacrificed at the end of exposure. A further 5 animals/sex/group were exposed for 90 days followed by recovery periods of 90, 10 and 360 days. The test substances were Cab-O-Sil (SAS 1; MMAD 2.08-3.04 µm and GSD 2.16-3.53) and OX50 (SAS 2; MMAD 1.30-2.20 µm and GSD 2.90-3.53. Nominal exposure concentrations were 0, 0.5, 1, 2.5 and 5 mg/m^3. Gross pathology of all organs was carried out, along with histopathology of the respiratory organs including lymph nodes, bronchoalveolar lavage (BAL) and collagen analysis of lung tissue.

There was no treatment-related mortality or statistically significant changes in body weight or food consumption in any of the exposure groups.

RAC highlighted the following effects of concern:

Text copied from pages 13-14 of the RAC opinion (ECHA, 2025)

Nasal cavities: Slight *mucosal degeneration* in high dose groups at the end of treatment; *Goblet cell proliferation* in levels 1 and 2 and nasopharyngeal duct at the end of treatment and after 3 months recovery in all groups; Higher incidences and severity of *hyaline inclusions in olfactory mucosa* in all exposed groups relative to the control; *Chitinase-positive crystals in olfactory mucosa*, levels 2-4, mainly in the high dose, SAS 1 treated animals.

Lymph nodes: *Granulomas* in ≥ 1 mg/m3 SAS 1 groups and in all SAS 2 groups, which were reversible after 6 months in the SAS 1 groups; *Granulomatous inflammation* at a minor severity in single males ≥ 2.5 mg/m3 SAS 1 groups, and in all SAS 2-treated groups; *Lymphoid hyperplasia* in most lymph nodes.

Lungs: *Discoloration or discoloured foci*, not reversible, in ≥ 1.0 mg/m3 SAS 2 groups, associated with inflammatory lesions, with dose-dependent incidence and/or severity; Increased *perivascular infiltration and bronchio-alveolar hyperplasia* in ≥ 1.0 mg/m3 SAS 1 groups and in all SAS 2 treated groups (reversible); *Hyperplasia* in the BALT (Bronchus Associated Lymphoid Tissue) in one SAS 2 0.5 mg/m3 (male) and in the SAS 2 group 2.5 mg/m3 (females); Minimal *macrophage agglomeration in the BALT* at 5.0 mg/m3 SAS 1, and in all groups exposed to SAS 2. *Granulomatous inflammation in the BALT* in animals treated with SAS 2. *Granuloma and fibrogenesis* effects as shown in the table below:

End of RAC text

Table 6: Granuloma and fibrogenesis observed in the lung, expressed in number of animals affected / mean severity from 0-4 in Fraunhofer ITEM (2019) taken from page 14 of the RAC opinion (ECHA, 2025)

	Dose	Air		SAS 1 0.5 mg/m³		SAS 1 1.0 mg/m³		SAS 1 2.5 mg/m³		SAS 1 5.0 mg/m³		SAS 2 0.5 mg/m³		SAS 2 1.0 mg/m³		SAS 2 2.5 mg/m³		SAS 2 5.0 mg/m³	
		M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F	M	F
3 months inhalation, n=10 animals/sex/dose	Granuloma (junct.)	0	0	0	0	2/1.0	0	4/1.0	0	9/1.0	9/1.0	9/1.2	5/1.6	6/1.7	6/1.5	9/1.2	6/1.5	9/1.2	5/1.2
	Masson T.: Fibrogenesis	2/1.0	1/1.0	0	1/1.0	3/1.0	1/1.0	6/1.0	5/1.0	8/1.0	7/1.0	7/1.0	9/1.0	6/1.0	7/1.0	7/1.0	9/1.0	10/1.0	7/1.0
3 months recovery , n=5 animals/sex/dose	Granuloma (junct.)	0	0	0	1/2.0	0	0	1/1.0	1/1.0	1/1.0	1/1.0	4/1.5	5/1.2	5/1.4	4/1.3	3/1.0	5/1.4	1/1.0	3/1.7
	Masson T.: Fibrogenesis	0	0	1/1.0	1/1.0	0	0	0	1/1.0	0	0	4/1.3	4/1.0	5/1.2	4/1.0	3/1.0	5/1.0	4/1.0	5/1.0
6 months recovery , n=5 animals/sex/dose	Granuloma (junct.)	0	0	0	0	0	0	0	0	0	1/1.0	0	3/1.0	2/1.0	4/1.0	4/1.0	5/1.2	5/1.2	5/1.0
	Masson T.: Fibrogenesis	0	0	0	0	0	0	0	0	0	0	3/1.3	1/1.0	4/1.8	2/1.0	5/1.2	0	5/1.4	5/1.4
12months recovery , n=5 animals/sex/dose	Granuloma (junct.)	0	0	0	0	0	0	0	0	1/1.0	0	0	2/1.0	0	0	1/1.0	1/1.0	3/1.3	2/1.0
	Masson T.: Fibrogenesis	2/1.0	0	2/1.0	0	0	0	0	0	0	0	0	2/1.0	0	1/1.0	4/1.0	4/1.8	5/2.0	4/2.0

p≤0.001 p≤0.01 p≤0.05 (Fisher's test)

RAC identified the effective doses as 2.5 and 0.5 mg/m^3 for SAS 1 and SAS 2, respectively.

A 13-week inhalation study was also available, comparable to OECD TG 413, with three different types of SAS: AEROSIL 200 (pyrogenic silica), Sipernat 22S (precipitated silica) and AEROSIL R 974 (surface-treated pyrogenic silica) (Reuzel, 1991). As surface-treated SAS was not within the scope of the CLH report, the results of treatment with AEROSIL R 974 were omitted from the assessment by the DS. Wistar rats (10/sex/dose) were exposed to AEROSIL 200 at 1, 6 and 30 mg/m^3 and Sipernat 22S at 30 mg/m^3 via inhalation for 90 days (6h/d, 5 d/wk). A further 5 animals/sex/group were included as 13, 26 and 39 week recovery groups, and 10 animals/sex/group were included as a 52-week recovery period. The MMAD of the test substances could not be determined.

No treatment-related mortality or clinical signs of toxicity were reported by the DS.

RAC identified effects in the lungs: accumulation of alveolar macrophages was observed in animals treated with both substances, and intra-alveolar polymorphonuclear leucocytic infiltration was observed in animals treated with AEROSIL 200. Further details are provided in Table 7.

Table 7: Summary of effects induced by AEROSIL 200 (pyrogenic silica) in number of animals affected, from Reuzel et al. (1991), taken from page 15 of the RAC opinion (ECHA, 2025)

		Males					Females				
Effects	Time after exposure (wk)	Control	1 mg/m³ AEROSIL 200	6 mg/m³ AEROSIL 200	30 mg/m³ AEROSIL 200	30 mg/m³ Sipernat 22S	Control	1 mg/m³ AEROSIL 200	6 mg/m³ AEROSIL 200	30 mg/m³ AEROSIL 200	30 mg/m³ Sipernat 22S
Accumulation alveolar macrophages	0	4	10	10	10	10	1	10	10	10	10
	52	1	1	1	10	4	0	1	4	8	0
IPLI (intra-alveolar polymorphonuclear leucocytic infiltration)	0	1	10	10	10	2	0	8	10	10	0
	52	0	0	0	0	0	0	0	0	0	0
Increased septal cellularity	0	1	10	10	10	2	1	9	9	10	6
	52	1	1	2	7	4	0	0	3	7	0
Alveolar bronchiolization	0	0	0	5	10	0	0	0	0	1	0
	52	1	2	0	1	1	0	1	0	2	0
interstitial fibrosis	0	0	0	0	0	n.d.	0	0	0	0	n.d.
	52	0	0	2	9	n.d.	0	1	1	10	n.d.

p≤0.001 p≤0.01 p≤0.05 (Fisher's test)

In the CLH report, the DS noted that the results of this study were later re-evaluated, and the pathology slides of males at 0, 13 and 52 weeks recovery were re-stained (Weber *et al.* 2018). The re-evaluation used a newer scoring system and concluded that no fibrosis could be detected in the slides, only macrophage aggregations and granulomas, which were reversible after 13-52 weeks. However, the DS referred to the recent RAC opinion on silanamine (ECHA, 2019), which identified several issues with the re-evaluation by Weber *et al.*, noting that: the re-evaluation was not conducted on all animals, and only one lung section per animal; de-slipping and re-staining of the cover slides could have damaged the tissue samples; the re-evaluation did not use Van Gieson stain to detect collagen and did not measure hydroxyproline; the recovery periods were unusually long for a 13-week study; and that RAC considered that reversible exposure-related fibrogenesis and structural remodelling of the lung tissue could not be excluded as an adverse effect with the potential to progress to fibrosis. RAC did not comment on the re-assessment by Weber *et al*. in their opinion on SAS.

RAC identified the effective doses in this study to be 1 and 30 mg/m^3 for AEROSIL 200 and Sipernat 22S, respectively.

Creutzenberg *et al*. (2022) reviewed a 90-day OECD TG 413 study, conducted by Anonymous (2014). Male Wistar rats (55/dose) were exposed to NM-200 (precipitated silica) via nose-only inhalation at 1, 2.5 and 5 mg/m^3 for 90 days (6 h/d, 5 d/wk), with a 90-day recovery period. The MMAD/GSD for the low, mid and high doses was 2.16 µm/0.09,

2.94 µm/0.2 and 3.12 µm/0.06, respectively. Histopathology was conducted on 10 animals/dose/time point.

RAC noted increased lung weights; these consisted of increased absolute weight in the high dose group 1 day after the end of exposure and in the mid and high dose group after 3 months of recovery, along with statistically significant increases in relative lung weights 1 day after the end of exposure in the mid and high dose groups. They also noted transient inflammatory effects in the lungs; the DS described these as animals in the mid and high dose groups showing significant increases in alveolar infiltration of granulocytes in the lungs, whilst high dose animals also showed increased interstitial macrophage infiltration and (multi)focal very slight alveolar granulocyte infiltration in the lungs. All lung effects were fully reversed after the recovery period.

RAC additionally highlighted persistent inflammatory responses in the nasal cavity, shown in Table 8.

Table 8: Nasal effects in rats exposed to precipitated silica from Anonymous (2014a); taken from pages 15-16 of the RAC Opinion (ECHA, 2025)

	End of treatment				End of recovery			
Doses (mg/m³)	Control	1	2.5	5	Control	1	2.5	5
Mucous cell hyperplasia (very slight)						3/10		
Mucous cell hyperplasia (slight)	1/10	10/10	8/10	2/9	3/10	3/10	10/10	6/10
Mucous cell hyperplasia (moderate)			2/10	7/9		2/10		3/10
Mucous cell hyperplasia (severe)								1/10
Hyperplasia of the respiratory epithelium (very slight)						1/10	2/10	4/10
Hyperplasia of the respiratory epithelium (slight)		2/10	5/10	9/9		5/10	5/10	6/10
Epithelial hyaline droplets (very slight)	3/10				7/10			
Epithelial hyaline droplets (slight)	1/10	10/10	9/10			9/10	10/10	2/10
Epithelial hyaline droplets (moderate)			1/10	9/9		1/10		7/10
Epithelial hyaline droplets (severe)								1/10
Multifocal epithelial (mixed) inflammatory cell infiltration (very slight)	1/10	10/10	6/10	2/9	2/10	6/10	8/10	8/10
Multifocal epithelial (mixed) inflammatory cell infiltration (slight)			4/10	7/9		2/10	1/10	2/10
Multifocal (chronic) inflammation of the nasal submucosal glands (slight)								1/10

Overall, RAC considered the effective dose in this study to be 2.5 mg/m^3.

Lastly, Lee and Kelly (1992) and Warheit (1991) described a 28-day study, in which male SD rats were exposed to LUDOX CL-X (colloidal silica) via the whole-body inhalation route at 10, 50 and 150 mg/m^3. The test substance had an MMAD of 2.9-3.7 µm and GSD of

1.9-2.3. A total of 25 animals were included in each dose group, with 10/dose sacrificed at the end of the exposure period, 5/dose subject to a 10-day recovery period and 10/dose subject to a 3-month recovery period. RAC noted the occurrence of increased lung weights, alveolar macrophage response, polymorphonuclear leukocytic infiltration and Type II pneumocyte hyperplasia in alveolar duct regions.

RAC considered the effective dose to be 50 mg/m^3.

Assessment of animal data

Effects observed in the four key animal studies included inflammation, granuloma and fibrogenesis in the lungs and inflammation of the nasal cavity along with alveolar bronchiolisation and lymphocyte invasion. RAC referred to Section 3.9.2.7.3 of Annex I to the CLP Regulation, which states:

Annex I, 3.9.2.7.3

Evidence from appropriate studies in experimental animals can furnish much more detail, in the form of clinical observations, haematology, clinical chemistry, and macroscopic and microscopic pathological examination, and this can often reveal hazards that may not be life-threatening but could indicate functional impairment. Consequently all available evidence, and relevance to human health, shall be taken into consideration in the classification process, including but not limited to the following toxic effects in humans and/or animals:

[…]

(d) significant organ damage noted at necropsy and/or subsequently seen or confirmed at microscopic examination;

(e) multi-focal or diffuse necrosis, fibrosis or granuloma formation in vital organs with regenerative capacity;

(f) morphological changes that are potentially reversible but provide clear evidence of marked organ dysfunction'

RAC considered the lung inflammation to be the most relevant effect for human health, particularly noting point (e) in the text above, which identified fibrosis and granuloma formation as toxic effects that should be taken into consideration in the classification. They referred to the epidemiologic literature (Hiraiwa and van Eeden, 2013), noting that there is a large amount of information available linking particulate exposure with cardiopulmonary morbidity and mortality mediated by inflammatory responses in the lungs.

Inflammatory effects in the form of hyperplasia and epithelial hyaline droplets were also observed in the nasal cavity in the studies by Fraunhofer ITEM (2019) and Anonymous

(2019); these were first observed at 0.5 and 1.0 mg/m^3 and increased in severity and incidence with increasing dose. RAC noted that not all studies performed histopathology of the nose, which could explain the incidental occurrence of nasal findings across the studies. RAC noted that relevance of nasal inflammation in rodents for human health was not as clear as lung inflammation, but nevertheless considered the nasal effects to be further indication that SAS causes non-adaptive functional impairment of the respiratory tract, and therefore also supportive of classification.

Animal studies were conducted with different types of silica, using different exposure concentrations, lengths of exposure and assessing different parameters. Therefore, RAC could not draw a conclusion on the relative toxicity of different types of SAS.

Effects were observed in the 90-d studies with pyrogenic and precipitated silica at concentrations as low as 0.5-2 mg/m^3 (Fraunhofer *et al.*, 2019; Reuzel *et al.*, 1991; Creutzenberg *et al*., 2022). These concentrations fell within the guidance values for Category 1 classification. Similarly, in the 28-day study key study (Lee and Kelly, 1992), effects were observed with colloidal silver at 50 mg/m^3, which also fell within the extrapolated guidance values for Category 1 classification. A comparison of the effective doses identified by RAC in the key studies and the guidance values for classification is provided in Table 9.

Table 9: comparison of effective doses in each of the four key animal studies to the guidance values for STOT RE classification, adapted from Table 4 of the RAC opinion (ECHA, 2025).

Study reference, type	SAS type, effective dose (mg/m^3)	Guidance value	Supported classification
Fraunhofer ITEM, 2019 **Rat, 90-d**	Pyrogenic SAS Cab-O-Sil/SAS 1: **2.5** OX50/SAS 2: **0.5**	Cat. 1: ≤ 20 20 < Cat. 2 ≤ 200	Category 1
Reuzel *et al.*, 1991 **Rat, 90-d**	Pyrogenic SAS AEROSIL 200: **1.0** Precipitated SAS Sipernat 22S: **30**	Cat. 1: ≤ 20 20 < Cat. 2 ≤ 200	Category 1
Creutzenberg *et al.*, 2022 **Rat, 90-d**	Precipitated SAS NM-200: **2.5**	Cat. 1: ≤ 20 20 < Cat. 2 ≤ 200	Category 1
Lee and Kelly, 1992; Warheit, 1991 **Rat, 28-d**	Colloidal SAS LUDOX-CL-X: **50**	Cat. 1: ≤ 60 60 < Cat. 2 ≤ 600*	Category 1

*Extrapolated guidance value according to Haber's rule; Table 3.6 of the Guidance on the Application of the CLP Criteria, Part 3 (ECHA, 2024b)

Overall, based on the effects observed in the four key animal studies, RAC concluded that SAS warranted classification as STOT RE 1. RAC agreed with the DS that it was not necessary to set an SCL.

Concerns raised during the public consultation

A large number of comments were received during the public consultation, from industry, MSCAs and individuals. Comments from MSCAs were generally in support of the Category 1 classification proposed by the DS, whilst comments from industry generally disagreed with the proposal. RAC responded to some of the concerns in their opinion.

Several comments were submitted expressing concerns that the effects of SAS were particle effects, rather than an intrinsic hazardous property, with commenters suggesting that they should not be used as the basis for classification under CLP. RAC responded to these concerns by referring to Article 1(1) of the CLP Regulation, which outlines the aim of the regulation: ensuring 'a high level of protection of human health and the environment'. They stated that classification should be based on scientific data demonstrating harmful effects, and therefore to neglect the findings described in the animal data above would be 'contrary' to the purpose of CLP in ensuring human health protection. RAC concluded that an adverse effect observed in an experimental study on a specific substance was sufficient to establish a link between the substance and the effect and thereby sufficient to potentially support classification. On this basis, RAC considered the results of the four key animal studies to be relevant for classification. Some of the comments also suggested that the effects seen in rats were not relevant to humans, owing to the fact that rats are more prone to developing an immune response to particles deposited in the lungs. However, RAC noted that alveoli clearance mechanisms and immunological responses are similar in rodents and humans. Additionally, SAS-related effects in the lungs were not specific to rats, with studies reporting effects in guinea pigs, rabbits and monkeys (Groth *et al*., 1981; Merget *et al.,* 1992). On this basis, RAC did not exclude the human relevance of the effects observed in rats in the key studies.

Other comments submitted during the public consultation included concerns relating to particle size, with commenters suggesting that the tested forms of SAS in the animal studies were not representative of SAS placed on the market, owing to the need for substances to be micronised to a respirable particle size in order to be compliant with standard inhalation toxicity test guidelines. RAC acknowledged that the aggregate size given in the EU REACH registration dossier was largely > 100 nm, but also highlighted that a small fraction of respirable aggregates are expected, and that there was no information available to conclude that the size listed in the REACH registration dossier was applicable to all forms of SAS.

Other comments stated that SiO_2 is 'generally recognised as safe' (GRAS) for use in food, pharmaceuticals and cosmetics. RAC acknowledged this argument, but also noted that CLP does not apply to medicinal products, food additives or cosmetics, and further noted that GRAS classification applies to oral administrations of a substance, not inhalable materials. Furthermore, RAC noted that, although SAS-containing products placed on the market may be considered safe, exposure to fine silica dust may be expected to occur during production or other reasonably expected use processes involving the substance.

Conclusion

Overall, RAC concluded that SAS should be classified as ***STOT RE 1; H372*** *(May cause damage to the respiratory tract via the inhalation route)*.

Classification proposed by the Agency:

The Agency cannot conclude on classification at this time.

The Agency is aware that extra scientific information not discussed in the RAC opinion is available. Therefore, to conduct a full assessment of all available data, synthetic amorphous silica will be assessed for STOT RE in a targeted Article 37A MCL proposal.

Germ cell mutagenicity

Not assessed in the CLH report or RAC opinion.

Carcinogenicity

Not assessed in the CLH report or RAC opinion.

Reproductive toxicity

Not assessed in the CLH report or RAC opinion.

Aspiration hazard

Not assessed in the CLH report or RAC opinion.

Environmental hazards

Hazardous to the aquatic environment

Not assessed in the CLH report or RAC opinion.

Other hazards

Hazardous to the ozone layer

Not assessed in the CLH report or RAC opinion.

Overall conclusion

The Agency has evaluated the RAC Opinion, its rationale and any additional scientific evidence that may have been made available to HSE against the criteria for classification and labelling in the GB CLP Regulation and technical guidance.

The Agency technical report **disagrees** with the classification proposed by RAC for the following hazards:

STOT RE:

The Agency cannot conclude on classification at this time. STOT RE will be assessed in a targeted Article 37A MCL proposal.

Overall, the conclusion is to **disagree** with the RAC opinion.

References

ECHA (2019) Committee for Risk Assessment (RAC) Opinion (including Annexes) proposing harmonised classification and labelling at EU level of Silanamine, 1,1,1-trimethyl-N-(trimethylsilyl)-, hydrolysis products with silica; pyrogenic, synthetic amorphous, nano, surface treated silicon dioxide; Reference CLH-O-0000006735-67-01/F; Date: 05/12/2019, Accessed date: 03/2026

ECHA (2024a) Guidance on the Application of the CLP Criteria, Part 2: Physical Hazards. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 4.0, ref: ECHA-24-G-07-EN. Available at https://www.echa.europa.eu/

ECHA (2024b) Guidance on the Application of the CLP Criteria, Part 3: Health Hazards. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 5.0, ref: ECHA-24-G-06-EN. Available at https://www.echa.europa.eu/

ECHA (2024c) Guidance on the Application of the CLP Criteria, Part 4: Environmental Hazards; and Part 5: Additional Hazards. Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures, version 4.0, ref: ECHA-24-G-05-EN. Available at https://www.echa.europa.eu/

HSE (2021) Agency technical report on the classification and labelling of Silanamine, 1,1,1-trimethyl-N (trimethylsilyl)-, hydrolysis products with silica; pyrogenic, synthetic amorphous, nano, surface treated silicon dioxide; Date: June 2021, Accessed date: 03/2026

HSE (2025) Agency technical report on the classification and labelling of: silanamine, 1,1,1-trimethyl-N- (trimethylsilyl), hydrolysis products with silica; Date: March 2025, Accessed date: 03/2026

For all other references, please see the EU CLH report and the EU RAC opinion (available at: https://echa.europa.eu/registry-of-clh-intentions-until-outcome)

CLH (2023) CLH report (including Annexes): Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. Substance Name: Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1] Silica gel, pptd., cryst.-free; Precipitated silica, silica gel, colloidal silica, amorphous, nano [2]; Date: 2023; Written by: The Netherlands Accessed date: 03/2026

ECHA (2025) Committee for Risk Assessment (RAC) Opinion (including Annexes) proposing harmonised classification and labelling at EU level of Silica, amorphous, fumed, cryst.-free; Pyrogenic, synthetic amorphous silica, nano [1] Silica gel, pptd., cryst.-free; Precipitated silica, silica gel, colloidal silica, amorphous, nano [2]; Reference CLH-O-0000007557-64-01/F; Date: 07/03/2025, Accessed date: 03/2026

Documents published as part of the EU CLH process: Source: European Chemicals Agency, http://echa.europa.eu/

Glossary of terms used in Agency technical reports

Agency, the	HSE, acting in its capacity as the GB CLP Agency
AR	Applied radioactivity
ATE	Acute toxicity estimate
BCF	Bioconcentration factor
BOD	Biological Oxygen Demand
bw	Body weight
CAR	Competent Authority Report
CAS	Chemical Abstracts Service
CI	Confidence interval
CL	Confidence limits
CLH	Harmonised Classification and Labelling
CLP	Classification, labelling and packaging (of substances and mixtures)
CO_2	Carbon dioxide
COD	Chemical Oxygen Demand
CV	Coefficient of Variation
d	Day
DAR	Draft Assessment Report
DOC	Dissolved Organic Carbon
DS	Dossier Submitter
DT	Dissipation time OR degradation time (also DissT or DegT where apparent)
DT_{50}	Dissipation half-life OR degradation half-life (hours or days), see also above
dw	Dry weight
ECHA	European Chemicals Agency
ECx	x% effect concentration
EFSA	European Food Safety Authority
E_rCx	x% effect concentration based on growth rate
EU	European Union
FEF_x	Forced expiratory flow at x% exhalation
FEV_1	Forced expiratory volume in 1 second
FVC	Forced vital capacity
GLP	Good Laboratory Practice
GRAS	Generally recognised as safe
GSD	Geometric standard deviation
H	Hours
HWSE	Healthy worker survivor effect

K_{OC}	Organic carbon-water partition coefficient
K_{OW}	Octanol-water partition coefficient
LC_x	x% lethal effect concentration
MCL	Mandatory Classification and Labelling
M-factor	Multiplying factor
MMAD	Mass median aerodynamic diameter
MW	Molecular weight
NOEC	No-observed effect concentration
OECD	Organisation for Economic Co-operation and Development
QSAR	Quantitative structure-activity relationship
RAC	Risk Assessment Committee
RAR	Renewal Assessment Report
RCOM	Response to comments document
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals regulation
SAS	Synthetic amorphous silica
STOT-RE	Specific target organ toxicity – repeated exposure
STOT-SE	Specific target organ toxicity – single exposure
TG	Test Guideline
US EPA	United States Environmental Protection Agency
wt	Weight
wwt	Wet weight

Further information

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