

Harmonised Classification Proposal for Synthetic Amorphous Silica (SAS) under CLP

ASASP Position following CARACAL 56 and 57 Discussions

Update May 2026

Purpose and status of this update

Following discussions at CARACAL and comments recently provided by ECHA, Member States and industry stakeholders, ASASP has further refined its position on the proposed harmonised classification of Synthetic Amorphous Silica (SAS) under CLP, incorporating additional scientific elements. While supporting the objective of a robust, science-based assessment, ASASP considers that key aspects of the current evaluation warrant further consideration.

1. ASASP position as presented at CARACAL

ASASP has consistently underlined that the current ECHA RAC Opinion on SAS contains fundamental scientific and regulatory limitations that require further clarification, notably related to substance identity and scope, mechanistic assumptions regarding silanol groups and ROS (Reactive Oxygen Species) and the human relevance of rat inhalation findings. ASASP reiterated at CARACAL that these scientific issues must be carefully considered to ensure a robust and scientifically sound basis for any potential harmonised classification. More broadly, these concerns point to limitations in the current CLP assessment framework, highlighting the need for a more tailored methodological approach to particulate materials before progressing further.

2. Updated scientific considerations following CARACAL discussions

Unclear substance identity and scope

Substance identity and scope remain insufficiently defined, notably due to the use of the descriptor 'nano' while extending the proposed classification beyond nanoforms, and the joint treatment of powders and colloidal dispersions despite different exposure profiles.

Biological mechanisms underlying rat specific alveolar macrophage overload in inhalation studies

Following the CARACAL discussions in January 2026 and the additional scientific material presented in March 2026, ASASP provides further clarification on the biological mechanisms of the rat inhalation of SAS particles (K. Weber et al., 2026, in preparation).



These findings raise questions regarding the adequacy of the current RAC Opinion, as they were not considered in its assessment.

After deposition of respirable particles in the alveoli, an active macrophage cleaning process is initiated. With the increasing uptake of particles together with proteinaceous fluid, alveolar macrophages progressively increase in volume, lose mobility, enter senescence and ultimately rupture within the alveolar lumen and the process is restarted by new naïve alveolar macrophages entering the alveoli. This process gives rise to the characteristic “foamy macrophage” morphology observed in rat inhalation studies.

New ultrastructural (SEM/EDX and SEM/TEM) evidence demonstrates that the morphological appearance of foamy macrophages is driven predominantly by fluid uptake rather than particle mass. At the terminal stage, a maximum of approximately 6% of macrophage volume consists of SAS particles bearing a lung surfactant/protein corona, while the remainder is composed of protein-containing fluid. Loss of motility, aging/senescence, cell death, rupture and release of cellular contents follow.

These findings confirm that alveolar macrophage overload is a volume-driven phenomenon, not a mass-driven one. For SAS, overload occurs when particle–fluid complexes reach approximately 1–6% of the volume of a naïve alveolar macrophage (typical diameter 12–15 µm). Critical determinants include aggregate and agglomerate density, re-agglomeration behaviour as shear forces decrease in the airflow, and dynamic solubility in biological fluids, which together govern deposition and clearance from the lung.

Importantly, enlargement of alveolar macrophages to diameters of up to approximately 80 µm is primarily triggered by fluid uptake, with particles playing a subordinate role. In rats, this enlargement results in physical obstruction of the alveolar lumen, progressive loss of macrophage mobility and the development of a self-perpetuating cycle (*circulus vitiosus*), whereby senescent macrophages rupture, release their contents and re-initiate the inflammatory process.

The *circulus vitiosus* has been demonstrated to be a rat specific phenomenon using appropriate histopathological marker technique. Due to fundamental anatomical and functional differences—most notably substantially larger alveolar dimensions and different clearance pathways—macrophage overload followed by alveolar obstruction does not occur in humans. As a result, the process is specific to rats and the failure mode observed in rats is not transferable to humans for SAS.

These additional data substantially reinforce the conclusion that the pathological changes observed in rat inhalation studies reflect a species-specific lung response mechanism, rather than an intrinsic, substance-specific hazard relevant for humans under normal and reasonably foreseeable exposure conditions.

3. Interpretation of lung-associated lymph node findings

Lung-associated lymph node findings observed in rat inhalation studies primarily reflect secondary responses to particle deposition and lymphatic clearance, rather than intrinsic toxicity of SAS. These responses are consistent with normal physiological processes for the transport and removal of respired particles.

Such findings are generally considered adaptive and non-adverse, in the absence of demonstrated functional impairment. Current evidence does not show that SAS-related lymph node changes lead to impaired immune function or systemic effects.

Moreover, lung-associated lymph nodes are anatomically distinct from the lung and belong to the lymphoid system. Their involvement should therefore neither be interpreted as evidence of toxicity to the respiratory tract, nor be used to extend the definition of the target organ.

Finally, lymph node effects are mechanistically linked to macrophage-mediated particle transport and rat-specific overload conditions, which strongly limits their relevance for human hazard assessment.

4. Exposure realism and test applicability

There is clear evidence that energy-intensive aerosolization of particles in inhalation studies is not representative of normal handling and use conditions for SAS. For low-density particulate materials, standard test approaches require careful interpretation to avoid artefacts driving regulatory conclusions.

5. Recommendations moving forward

Building on these discussions, ASASP invites consideration of whether the current RAC Opinion adequately reflects recent scientific clarification on rat-specific lung overload mechanisms; whether classification can proceed without a clear substance scope; and whether further methodological reflection on particulate materials would be appropriate prior to advancing harmonised classification.

In this context, ASASP takes note of and welcomes the recent Agency [technical report](#) by the UK Health and Safety Executive (HSE, April 2026), which concluded that no classification for STOT RE can be determined at this stage for synthetic amorphous silica and identified the need for further targeted assessment of all available scientific evidence before any regulatory conclusion is reached.

6. Concluding remark

ASASP supports a science-based and proportionate application of CLP and remains committed to constructive engagement with Member States, the Commission, and ECHA on the assessment of particulate materials such as SAS.

In line with this position and considering the need identified for further expert input in this area, ASASP proposes the establishment of a dedicated expert group on particulate materials which would provide an appropriate framework to address key methodological aspects, including particle characterisation, exposure relevance and interpretation of inhalation studies and thereby support a consistent and transparent application of CLP. This request aligns with the recommendations of the Particles Platform for the creation of an expert group on particles under the auspices of ECHA, composed of representatives from ECHA, academia, and industry.

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