Our position regarding colloidal silica and nanoparticles

Bohus, Sweden, April 23rd, 2019

- **At Nouryon (former AkzoNobel Specialty Chemicals) we recognize that new methods may need to be developed to assess and control the potential risks of new technologies.**
- **Overall, amorphous colloidal silica is an old technology while modern "nano" colloidal silica products are manufactured to have specific properties.**
- **We have commissioned several acute inhalation toxicity studies with modern colloidal silica products, and results confirm that these materials are not dangerous to health when inhaled.**
- **We have recently completed an in vitro dermal penetration study demonstrating that the absorption of colloidal silica through the human skin is negligible.**
- **We have also conducted a Local Lymph Node Assay and several in vitro genotoxicity assays on a surface modified colloidal silica showing no sensitization and no genotoxic effects.**
- **Several decades of working with and handling these products support our conclusion that colloidal silica can be used safely when handled as recommended by Nouryon.**

In line with the CEFIC Position paper on nanomaterials, Nouryon acknowledge that the development and application of nanotechnology can raise safety, societal, and regulatory questions and challenges.

Although we believe that the existing methods in principle provide a suitable framework for the hazard assessment of nanomaterials, we recognize that new approaches and methods may need to be developed to assess and control the potential risks of such newly emerging technologies.

In use for decades
Colloidal silica meets the size definition for nanoparticles[1] and is manufactured using technology based on chemical understanding and techniques that date back to the early 1950s.So in fact, this particular nanotechnology has been with us for many decades. Engineering improvements allow much better control over the manufacturing process and thus much better product control. In addition, chemical innovations developed over time now allow us to devise and manufacture surface-modified colloidal silicas that meet specialized customer requirements. Overall, this is an old technology which has been improved to produce modern products, differing from the old ones in certain technical aspects, but to the best of our knowledge, not different with respect to the absence of toxicological hazards.

Modern "nano" colloidal silica products are designed to have specific properties and represent the continuation of decades of development. Colloidal silica products have been widely used in a variety of industries for decades. Although in the nanoparticle size range, colloidal silica products have a much longer history of safe, widespread use than recently invented nanomaterials, such as carbon nanotubes or quantum dots.

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Amorphous colloidal silica
All colloidal silica dispersions are nanoparticles per definition, otherwise they would not be sols (stable colloidal dispersions). On the other hand, if dried these small particles irreversibly aggregate into much bigger agglomerates and aggregates of sizes in the micrometer range. The amorphous nature of colloidal silica has been extensively assessed through X-ray diffraction. Analytical reports are available for a variety of colloidal silica grades.

Inhalation studies
Nouryon has commissioned several acute inhalation toxicity studies with modern colloidal silicas, and data from these studies confirm that these materials are not dangerous to health when inhaled.

The studies were performed according to standard OECD testing guideline 403 under quality assurance according to GLP. As required, testing conditions were carefully chosen to ensure that the material would get deeply into the lungs by delivery as a respirable liquid aerosol with droplet size less than 3 micrometer MMAD (Mass Median Aerodynamic Diameter). Steps were taken to prevent, as much as possible, that the silica nanoparticles would form larger-than-nanosize aggregates.

Under these conditions, the acute 4-hour $LC50_2$ values of the four tested colloidal varieties were all higher than 5000 mg/m_3 (dry silica weight). This means that these materials are not considered to be dangerous to health by inhalation, according to standards accepted worldwide.

Studies on subchronic and chronic pulmonary toxicological effects of inhaled amorphous silica particles are available, though not specifically for colloidal silica. The results of these studies indicate that animal exposure to amorphous silica leads to transient pulmonary changes but not to chronic conditions (Groth et al. 1981; Reuzel et al. 1991; McLaughlin et al. 1997; Johnston et al. 2000; Warheit 2001; Merget et al. 2002; Greer and Goldsmith 2007). The fact that pulmonary changes are transient is probably partly due to amorphous silica being weakly soluble in biological fluids and thus slowly disappearing from the lungs. In the repeated inhalation toxicity studies, levels of 1-10 mg/m3 were found to be at the NOAEL (No Observed Adverse Effect Level). At present there is no reason to assume that Nouryon's colloidal silica dispersions would behave differently.

The acute inhalation toxicity tests described above represent a worst-case scenario; Nouryon is confident that under normal conditions of use in hard surface cleaning applications, the aerosol droplet size will not reach respirable dimensions in sufficient amounts and that the concentration of respirable particles in air will be orders of magnitude lower than 1-10 mg/m_3. The long-term inhalation toxicity tests in animals with respirable particles indicate that amorphous silica does not cause chronic toxicity if repeatedly inhaled at low concentrations, i.e. at concentrations of about 1 mg/m_3. In addition, epidemiological studies do not indicate that amorphous silicas have any relevant potential to induce fibrosis in exposed workers (ACGIH 2001). Therefore, Nouryon believe that the use of our colloidal silica products in every application we recommend is safe.

Other studies
Skin exposure to colloidal silica may occur when handled and used in different sorts of applications. A recent in vitro study performed by Nouryon on four different types of colloidal silica (including unmodified and modified silica) shows that the dermal absorption of silica from potential exposure to any of these formulations would be negligible.

<u>Sensitization</u>
A recently performed LLNA study (OECD 429) on a surface modified silica shows that the substance has a Stimulation Index (SI) lower than 3 and is therefore not considered to be a sensitizer.

Genotoxicity

Three new in vitro genotoxicity studies (OECD 476, 471 & 487) were recently performed on the same modified silica product showing that the substance has no genotoxic potential at all.

In the paper industry, exposure to colloidal silica based nanoparticles is limited to its use in the paper machine; once dried, colloidal silica is not present as nanoparticles in the final product. Therefore, exposure to nanoparticles of colloidal silica is limited to site operations, which are well controlled through good manufacturing practices and industrial hygiene measures.

As yet unpublished studies with size-controlled nanosized colloidal silica, both uncoated, 12nm diameter and Al-coated, 50-70 nm diameter, indicate that the acute aquatic toxicity of these particles is low (algae 72-h EC50, growth rate > 100 mg/L; Daphnia 48-h EC50 > 100 mg/L). There are also strong indications that these particles adhere strongly to organic matter in suspension, which should lead to rapid clearance in waste water treatment installations. Taken together, this confirms our previous position that modern colloidal silica should be considered environmentally safe.

Risk characterization not required

In February 2009, the consortium for Synthetic Amorphous Silica announced the successful submission of a dossier covering several forms of silica, including colloidal silica, to the European Chemicals Agency (ECHA). The Registration Dossier prepared by this consortium was made available at the end of 2010 and the overall conclusion of the Hazard and Exposure Assessment and Risk characterization contained in the Chemical Safety Report is that “Based on available data, synthetic amorphous silica is not a hazardous substance. Therefore, in line with REACH, further exposure assessment and risk characterization are not required”.

The research on toxicity of nanoparticles is in its infancy, and existing standard toxicity tests need to be carefully designed or modified to ensure that the outcome is indeed related to particle size. However, many nanoparticles will agglomerate into larger aggregates for which standard toxicity testing can be applied.

Meanwhile, based on several decades of working with and handling these colloidal silica products, and from the recent information update provided by the REACH registration, we believe that colloidal silica can be used safely in applications recommended by AkzoNobel Pulp and Performance Chemicals.

ECHA evaluation decision as per art. 46 of REACH, contested by Industry

In March 2015, ECHA published a decision on the evaluation of synthetic amorphous silica requesting additional information on physico- chemical properties, subchronic toxicity data and uses of all forms of silica (products). A large number of silica producers, including Nouryon, decided to contest the decision before the Board of Appeal. The Board of Appeal has considered the case to be admissible and the appeal is now being processed. A final decision from the Board is expected in some months from now.

[1] The ISO standard refers to engineered nanomaterials with particles where one or more external dimension is in the size range of 1- 100 nm. More recently the EU recommendation EC 2011/696/EU has included aggregates and agglomerates of nanoparticles and extended the scope to naturally occurring substances. This new definition has not reached consensus among industry experts.

[2] LC50 is the concentration in air at which 50% of test animals die either during the 4-hour test or during a following 14-day recovery period. In fact, the 4-hour LC50 could not be established since no animals died in three out of four tests (CC30, i.e. surface-modified silica), and only 2 out of 10 animals died in the fourth (conventional colloidal silica).

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RCC Study Number B13230 - Bindzil 30/360: 4-Hour Acute Inhalation Toxicity Study in rats

RCC Study Number B13206 - Bindzil CC30 Methanol free: 4-Hour Acute Inhalation Toxicity Study in Rats

RCC Study Number B13217 - Bindzil CC30 Ethanol-Based: 4-Hour Acute Inhalation Toxicity Study in Rats

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National Research Centre for the Working Environment, Denmark fact Sheet No 58

Will Research Project Number 507791
Assessment of contact hypersensitivity to Bindzil CC 301 in the mouse (Local Lymph Node Assay)

Will Research Project Number 507691
Evaluation of the mutagenic activity of Bindzil CC 301 in an in vitro mammalian cell gene muatation test with L5178Y mouse lymphoma cells

Will Research Project Number 507689
Evaluation of the mutagenic activity of Bindzil CC 301 in the salmonella thyphimurium reverse mutation assay and the escherichia coli reverse mutation assay

Will Research project Number 507812
An in vitro micronucleus assay with Bindzil CC 301 in cultured peripheral human lymphocytes

Questions & Answers: Amorphous silica behaviour

The following paragraphs summarize the behaviour of silica in different applications and the likelihood of human exposure to nanoparticles.

Paper applications

1. Do any nanosized particles remain on the sheet after paper has been dried? How complete is the agglomeration? Is there a residual amount that does not agglomerate?

When silica nanoparticles are dried almost all the nanoparticles agglomerate irreversibly to big aggregates. When the nanoparticles come into close contact during the drying process strong siloxane bonds are formed between the particles due to the relatively high solubility of silica (in contrast to many other nanoparticles).

2. How stable are the dried agglomerates found in a sheet of paper? Can nanosized particles be reformed from the dried agglomeration during any downstream paper converting operations, such as folding, cutting, gluing, printing, wetting or heating?

When trying to de-agglomerate the dried particles with various techniques it could easily be shown with particle size measurements (light scattering) that the original size cannot be recreated.

3. If there are nanosized particles in a sheet (either residual from incomplete agglomeration or formed due to instability of the agglomerates), can they be released from the sheet during downstream operations such as folding, cutting, gluing, printing, wetting or heating?

As mentioned previously, almost no nanoparticles remain and it is impossible to reform them.

Other applications such as coatings (e.g. plastic or metal surfaces), binder uses (e.g. precision casting moulds, ceramics), flocculation (e.g. fining of beverages) or semiconductor polishing (e.g. silicon bare wafers)

1. How complete is the agglomeration of amorphous silica (SiO_2) particles, when colloidal silica is dried as supplied after being spilled or as part of a coating formulation together with organic polymers?

When silica nanoparticles are dried almost all the nanoparticles agglomerate irreversibly to big aggregates. When the nanoparticles come into close contact during the drying process, strong siloxane bonds are formed between the particles due to the relative high solubility of silica (in contrast to many other nanoparticles).

2. How stable are the dried agglomerates found on different substrates? Can nanosized particles be reformed from the dried agglomeration during any mechanical operations of a coated surface, such as wiping, folding, cutting, gluing, printing, wetting or heating?

When trying to de-agglomerate the dried particles with various techniques it can easily be shown with particle size measurements (light scattering) that the original size cannot be recreated.

3. Does sanding dust from paints, lacquer and filler containing nanoparticles pose a risk?

A recent publication of the National Research Centre for the Working Environment in Denmark shows that the addition of nanoparticles does not increase the adverse effects of sanding dust from paint, lacquer and fillers. As a matter of fact the results indicate that the matrix itself (paint, lacquer or filler) has a greater impact on the adverse effects than the addition of nanoparticles.

4. If there are nanosized particles in a coating or any other form of dried layer (either residual from incomplete agglomeration or formed due to instability of the agglomerates), can they be released from the sheet during downstream operations, such as folding, cutting, gluing, printing, wetting or heating?

As mentioned previously, almost no nanoparticles remain and it is impossible to reform them.

Household applications; hard surface cleaning agents

1. Are silica nanoparticles present in sprayable versions of cleaning products? Is there a risk of inhalation of silica particles and if so, will these nanoparticles penetrate deep into the body?

Silica nanoparticles are present in formulations for hard surface cleaning. These formulations are applied on the surface using spray nozzles that release droplets of > 100 microns. These droplets can contain non-agglomerated silica particles; however considering the size of the droplets they will not reach the lungs. They will be deposited in the respiratory tract, ingested and finally cleared via the gut.

2. What happens when the product is applied on a hard surface?

When the product is applied on the surface it will form a film and dry out. When silica nanoparticles are dried almost all the nanoparticles agglomerate irreversibly to big aggregates. When the nanoparticles come into close contact during the drying process strong siloxane bonds are formed between the particles due to the relatively high solubility of silica (in contrast to many other nanoparticles).

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