EFSA Stakeholder Workshop on
Nanoscience and Nanotechnology

Physical chemical Characterization of Nanomaterials

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aSASp Association of Synthetic Amorphous Silica Producers

A sector group of Cefic

European Chemical Industry Council - Cefic aisbl

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ASASP is formed by the nine leading Synthetic Amorphous Silica

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Main Goals of ASASP

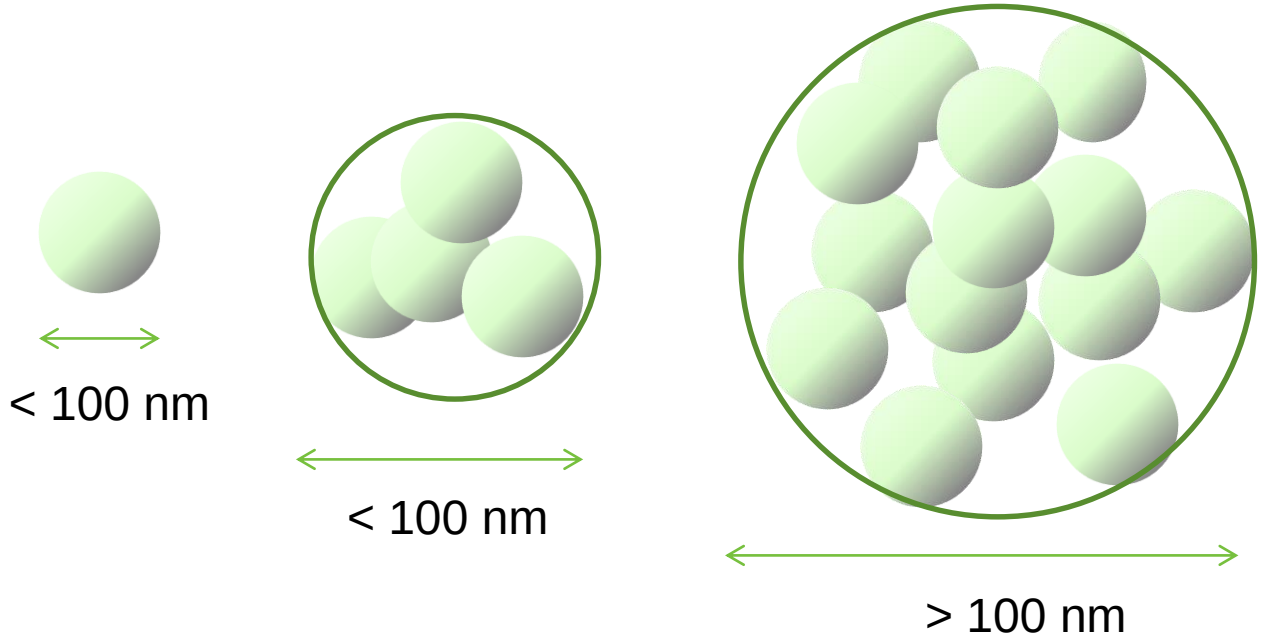
- Promote the safe use and benefits of SAS to society
- Be the scientific knowledge leader for the safety, health and environmental matters of SAS
- Actively follow, engage and ensure compliance with all common regulatory issues affecting SAS
- Communicate knowledge about SAS in appropriate ways to all interested parties

Crunch Points

- What is a particle versus a nano particle / primary particle / constituent particle?
- Aggregate breakdown by mechanical or biological forces
- Dissolution / Solubility of nanomaterials

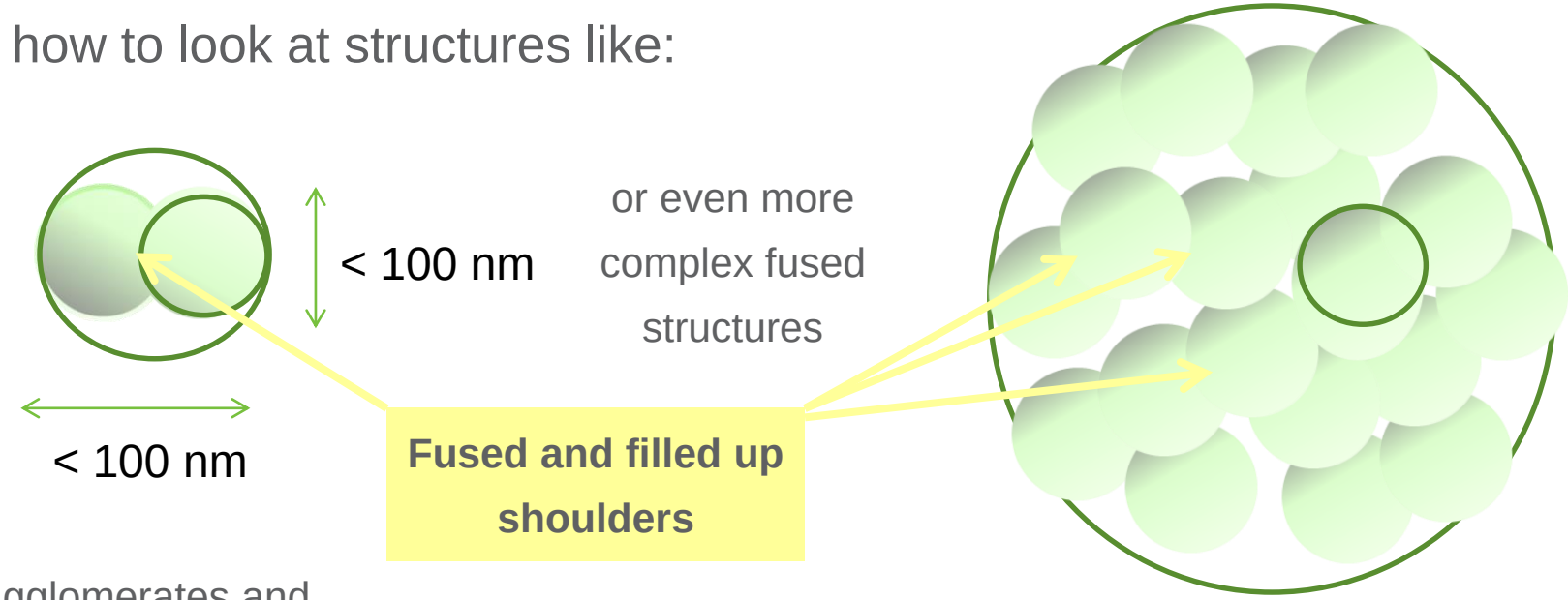
EFSA – 1.2.2 Definition of Nanomaterial

"… *For the purposes of the recommended definition, 'particle' means a minute piece of matter with defined physical boundaries, 'agglomerate' means a collection of weakly bound particles or aggregates where the resulting external surface area is similar to the sum of the surface areas of the individual components, and 'aggregate' means a particle comprising of strongly bound or fused particles.* … (Guidance page 11)"



EFSA – 1.2.2 Definition of Nanomaterial

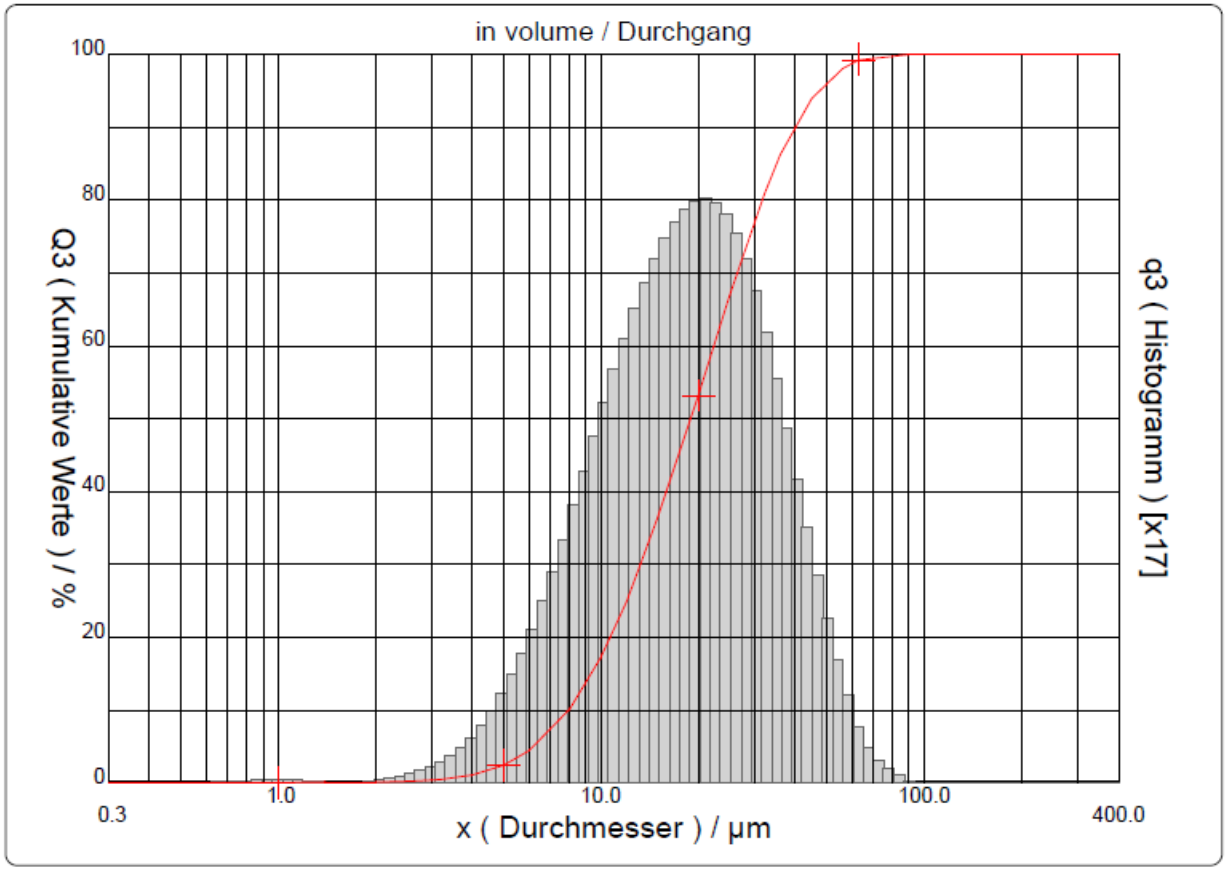
But - how to look at structures like:



TEM pictures by Evonik Industries

Physical chemical Characterization of Nanomaterials

Typical particle size distribution of precipitated Silica aggregates measured in an aqueous dispersion with Laser Diffraction. Agglomerates are deagglomerated using ultra sonic bath for 60 sec.



CILAS 920 Wet

0.3 to 400 µm

Measured in 30 intervals

Data provided by Grace GmbH

Suggested Energies for treating aggregates in Water

Ultra Sonic

200 W for 9 min

resulting in 108 KJ

Sample size:
100 ml H_2O

1 g sample

for analysis

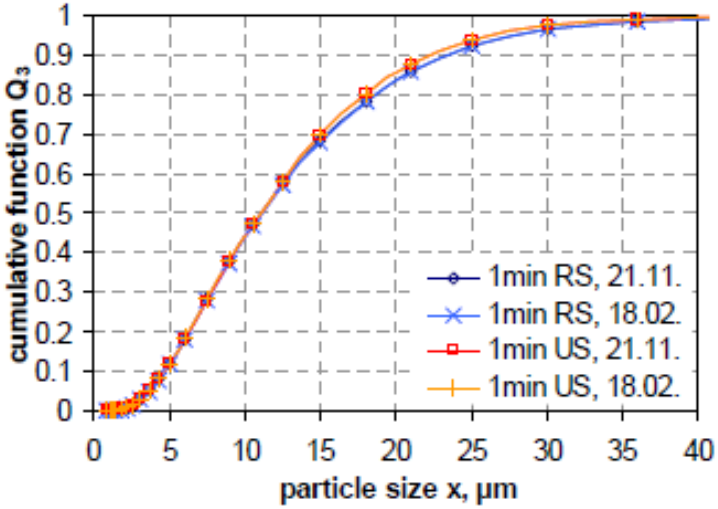
Induced energy is transformed into heat

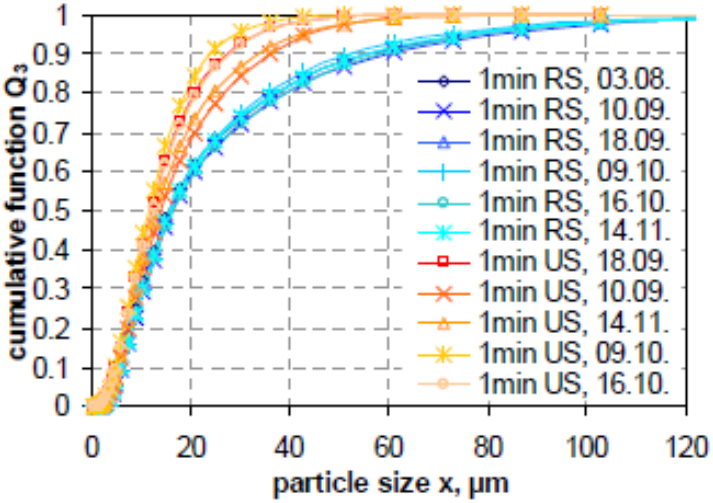
With a sample temperature of 20°C, 33,44 kJ will rise the temperature to the boiling point of water. The remaining 74,56 KJ will evaporate approx. 33 g of the 100 ml of water. Thus the sample must be prepared in an ice bath, beside all other issues with the ultra sonic finger.

Investigation of potential Aggregate Breakdown

- Aggregate breakdown may happen however can not be assumed in general and are strongly related to the induced energy and the substance
- Weak energy exposure in most cases is not sufficient to change aggregate size while intensive energy expose may create this effect but the amount of energy is not typical for biological systems

Laser Diffraction results of weakly and intensively dispersed powder materials





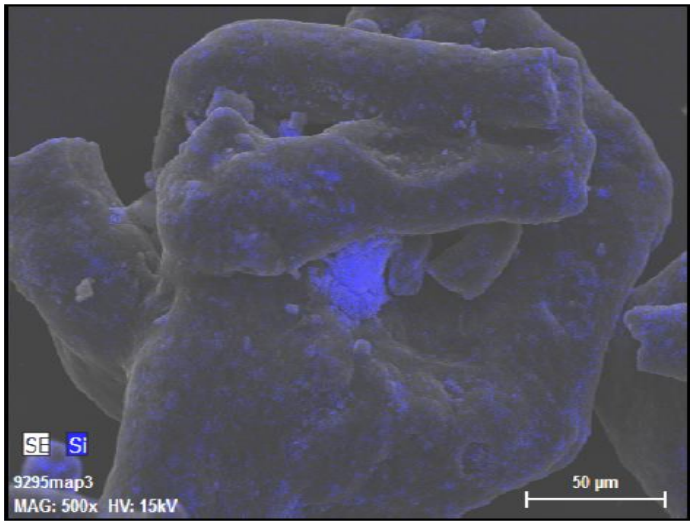
RS = dispersed with **R**otor **S**tator System; **US** = dispersed with **U**ltra **S**onic System

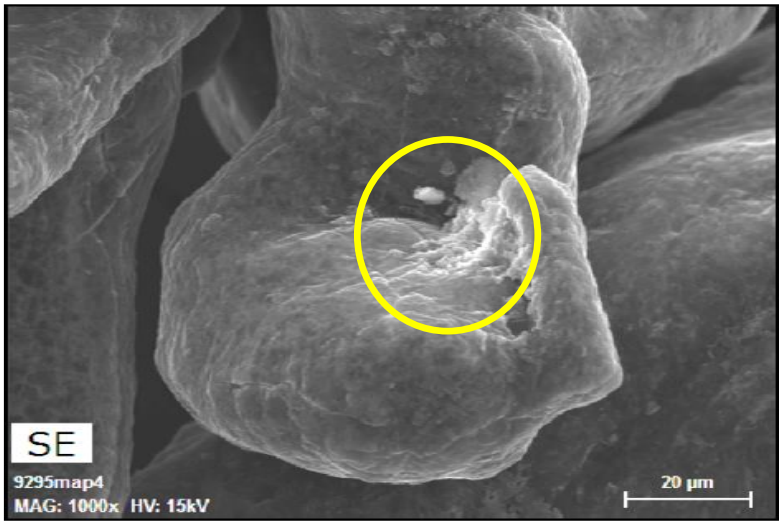
Measurements by the University of Dresden Prof. Dr. M. Stintz

Investigation of potential Aggregate Breakdown

- During technical application the agglomerates are broken down but the induced energy is normally not sufficient to break down the existing aggregates into smaller particles or even into the constituent particles
- Only aggregates acting e.g. as free flowing agents, as a certain size of the particles is needed

Example of Silica on a tomato powder particle acting as free flowing agent





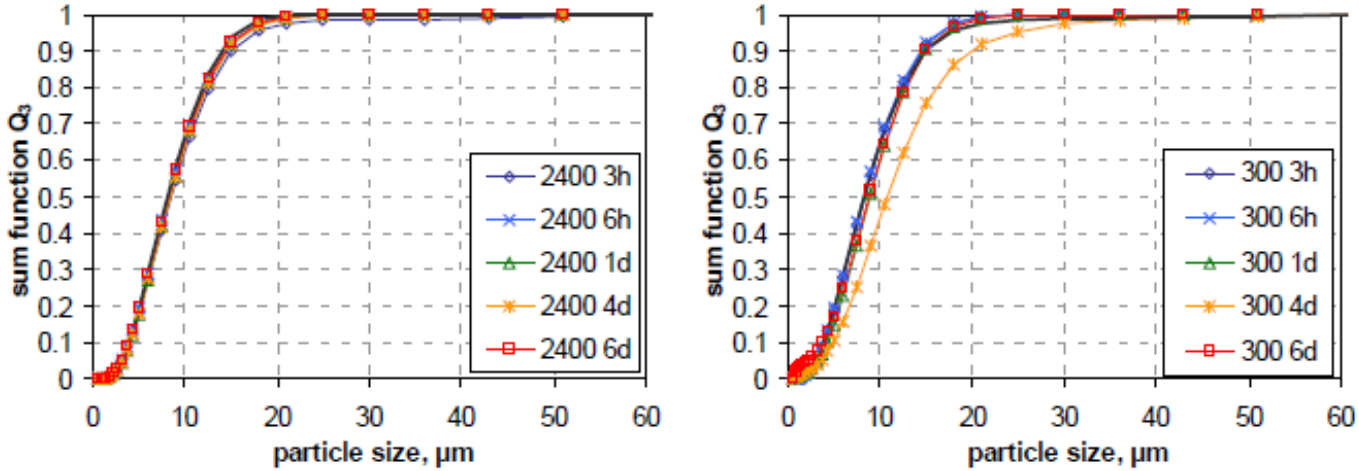
SEM with **EDX = S**canning **E**lectron **M**icroscopy with **E**nergy **D**ispersive **X**-ray spectroscopy

Measurements by the University of Dresden Prof. Dr. M. Stintz

Investigation of potential Aggregate Breakdown

- A specific designed test for powders showed no evidence for the analyzed powder that a physiological medium containing a lung surfactant actively disaggregates aggregates into the forming constituent particles
- Aggregate stability in liquid media is a typical substance intrinsic property

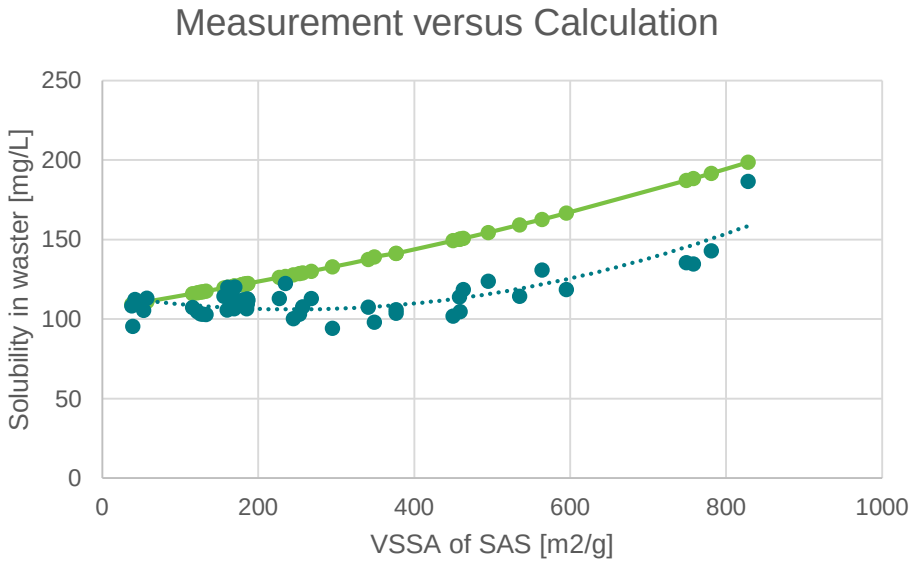
Evolution of Laser Diffraction size distribution for 2,4 mg/mL and 0,3 mg/mL exposed to lung surfactant (DPPC)



Measurements by the University of Dresden Prof. Dr. M. Stintz

Dissolution / Solubility of nanomaterials

- Solubility is an intrinsic substance property
- Solubility is a function of temperature, pH, shape of the particles, the solvent (water/ethanol/biological media) and time
- Solubility versus disaggregation
- Solubility / Hydrolysis / Transformation Dissolution



From ASASP Cosmetic Dossier submitted to DG GROW

Solubility of different forms of one substance under uniformed conditions (temperature, mass/liter of water, pH range). Tyndall Effect was used to demonstrate solubility instead of disaggregation. Time to reach the equilibrium according to OECD 105 is 2 to 3 days in a static system.

EFSA Dissolution Rate of Nanomaterials

EFSA Guidance Paper page 40:

- "Information on the dissolution rate for each nanomaterial should be obtained from:
  - At least four time points for the intestinal phase (of up to 4 h) to allow the determination of a dissolution rate.
  - A minimum of duplicate samples at each time point should be used.
  - At least three different concentrations with a middle concentration that is calculated to be representative for human exposure should be used.
- A nanomaterial is considered to dissolve quickly/have a high dissolution rate if 12 % or less of the material (mass based) is present as particles after 30 min of intestinal digestion compared to the particulate concentration at the beginning of the in-vitro digestion."

Conclusion

- Aggregates are usually an extremely stable structure and cannot easily disaggregated into constituent particles by mechanical forces
- Test of different forms of one substance did not show any disaggregation of aggregates in a biological medium (here lung surfactant)
- EFSA expected time range of 30 min for the dissolution (mass based) of 88 % is unlikely for most inorganic nanomaterials

Questions?