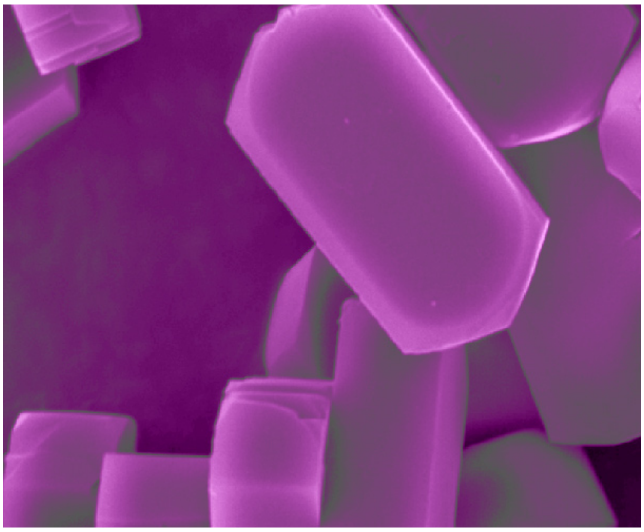
ENPRA Risk Assessment of Engineered NanoParticles



Environmental, Health and Safety Impacts of Nanoparticles

European Observatory on NanoSafety

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Electron microscopy images of silica particles (zeosil). Reprinted with permission from Particle and Fibre Toxicology 7, 39 (2010). Copyright 2010 Napierska et al; licensee BioMed Central Ltd.
To see also: "Katholieke Univ. Leuven & Univ. Catholique de Louvain: Relationship between physicochemical properties and nanosilica toxicity" on page 9.

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Environmental, Health and Safety Impacts of Nanoparticles

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Introduction

The fourth meeting of the European Observatory on NanoSafety (EONS) has been held in Brussels on March 31, 2011. The present report compiles the articles' presentations and the discussions developed during this event.

About the European Observatory on NanoSafety

The European Observatory on NanoSafety (EONS) is a collective initiative launched in 2009 by the Observatory for Micro&Nanotechnologies (OMNT) and the European consortium ENPRA (Risk Assessment of Engineered NanoParticles). Every 6 months, EONS meetings bring together experts in environmental health and safety issues related to nanoparticles and nanomaterials (including OMNT experts, partners of the ENPRA project and invited key scientists) and provide them with the unique opportunity to collectively review and comment the latest research progresses of the domain. Topics addressed by the panel cover the full scope of 'NanoSafety' including detection and characterization of nanomaterials, toxicology, ecotoxicology, risk assessment and risk management as well as normative and regulatory aspects. Proceedings of the meetings are published by the OMNT.

NIOSH, Karolinska Inst. & Univ. of Pittsburgh: Comparison of the genotoxic potential of carbon-based nanofibers, single-walled carbon nanotubes and asbestos

Reviewed by R. Schins

Carbon nanofibers, carbon nanotubes and asbestos: ranking their genotoxic potency

There has been a steady increase in the interest of carbon nanofibers (CNF) by industry. Compared to carbon nanotubes, CNF are relatively cheap to produce. They are used in particular in composite materials for the improvement of strength, durability, heat resistance and conductivity. However, despite their increasing use, to date only few toxicological studies have been performed with CNF.

In the present study from the **National Institute for Occupational Safety and Health**, the **Karolinska Institute** and the **University of Pittsburgh** the genotoxic potential of CNF in vitro has been addressed in comparison to single-walled carbon nanotubes (SWCNT) and of crocidolite asbestos fibres. A well-characterised heat-treated CNF sample (Pyrograf®-III, median aspect ratio: 500) was evaluated along with a sample of SWCNT (mean aspect ratio: 1000) and the IUCC crocidolite asbestos reference sample (mean aspect ratio: 30). Genotoxicity was evaluated in V79 Chinese hamster lung fibroblasts by the alkaline comet assay and the micronucleus (MN) test (Figure 5). The relative contribution of clastogenic versus aneugenic effects to MN-formation was addressed in SAEC human small airway epithelial cells using fluorescence in situ hybridisation (FISH). Parallel experiments described in the paper revealed CNF uptake and reactive oxygen species (ROS) formation in RAW267.4 mouse macrophages, as determined by transmission electron miscroscopy (TEM) and electron spin resonance (ESR), respectively.

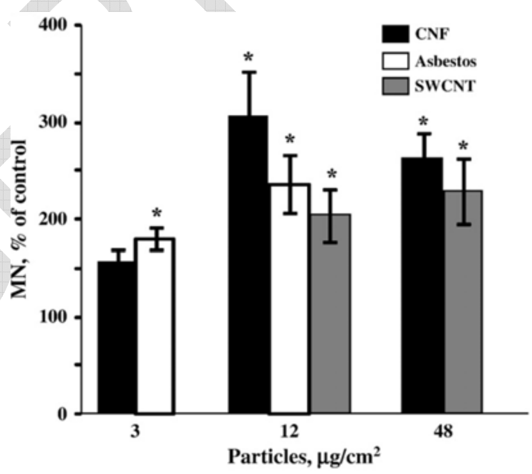

Figure 5: Induction of micronucleus (MN) in V79 cells after treatment with CNF, crocidolite asbestos or SWCNT.
Reprinted with permission from Toxicology and Applied Pharmacology 252, 1 (2011). Copyright 2011 Elsevier.

The study demonstrates that CNF have a genotoxic potential and also reveal that the effects of the specific CNF sample were generally stronger than that of both SWCNT and crocidolite, when compared on a mass concentration basis. Evaluation of CNF-treated SAEC cells by MN-FISH analysis showed that both clastogenic and aneugenic effects occurred, although the high proportion of centromere-positive MN indicated that aneugenicity is dominating.

The paper provides important novel information on the potential genotoxic action of CNF. The study findings are also in support of the hypothesis that genotoxic effects of high aspect ratio nanomaterials may involve two different mechanisms, namely (1) ROS generation leading to DNA strand breakage and (2) physical interference with DNA/chromosomes and/or the mitotic apparatus resulting in chromosomal malsegregation.

Some concern was expressed about the fact that the MN-test was not entirely performed according to the currently recommended guidelines. Moreover, it should be noted that the genotoxic effects versus uptake and ROS formation were measured in different cell types.

"Genotoxicity of carbon nanofibers: are they potentially more or less dangerous than carbon nanotubes or asbestos?" ; E.R. Kisin, A.R. Murray, L. Sargent, D. Lowry, M. Chirila, K.J. Siegrist,

D. Schwegler-Berry, S. Leonard, V. Castranova, B. Fadeel, V.E. Kagan, A.A. Shvedova : ***Toxicology and Applied Pharmacology*** **252**, 1 (2011).

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Risk Assessment & Risk Management

RIVM, Phillips Research & RIKILT: Nanosilica in food. Analytical characterisation and risk assessment

Reviewed by K. Aschberger

Nanosilica: a risk from our diet?

This paper by researchers from the **RIVM**, **Phillips Research** and the **RIKILT** describes a risk assessment appraisal for one important nanomaterial used in food products. For the exposure assessment, the presence, particle size and concentration of nanosilica were analysed in several food products. As an example Figure 8 shows the presence of silica nanoparticles in a sample of coffee containing powdered creamer. Based on these measurements and consumption data the intake of nanosilica via food was estimated to be 124 mg/day (1.8 mg/kg bw/day). The contribution of each product to the total nanosilica intake was estimated (Figure 9). For the hazard assessment there is only limited data publicly available on the kinetics and toxicity of nanosilica, suggesting that nanosilica becomes bioavailable to some degree and can exert toxicity on the liver, with higher potency for the nano-form than for the non-nanoform.

Scenario 1 assumed that all nanosilica particles were dissolved in the gastrointestinal tract (GIT) and absorbed as dissolved silica. The risk assessment for systemic effects was based on hazard data with non-nanosilica (No Effect Level or NEL: 625 mg/kg bw/d from a chronic study) and concluded with no risk.

Figure 8: Presence of nanosilica particles (peak) in coffee sample containing powdered creamer as identified by mass spectrometry (HDC-ICPMS chromatograms).
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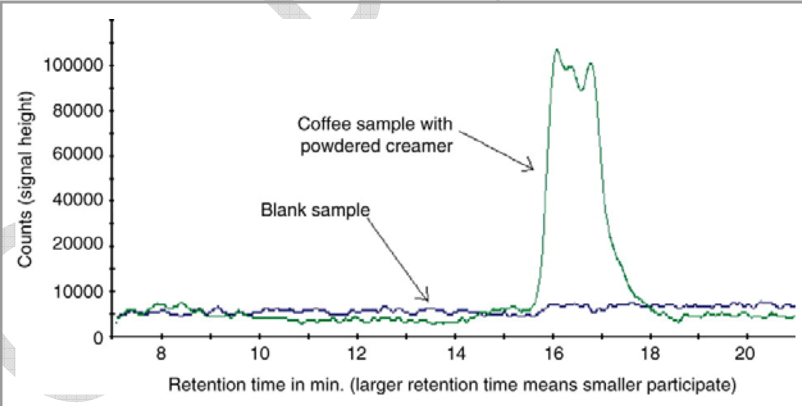

The second scenario assumed that nano-silica was absorbed as particles from the GIT and a Lowest Observed Adverse Effect Level (LOAEL) of 1500 mg/kg/bw/d from a 10 week with nanosilica study was used. This scenario however included too many uncertainties with regard to limited toxicity data, the most appropriate dose metrics, the nanosilica characteristics and the assessment factors, to draw any conclusion.

Figure 9: Contribution (expressed as %) of each product included in the study to the estimated total nanosilica intake. Products that contribute to less than 3% (each) are classified as "Others".
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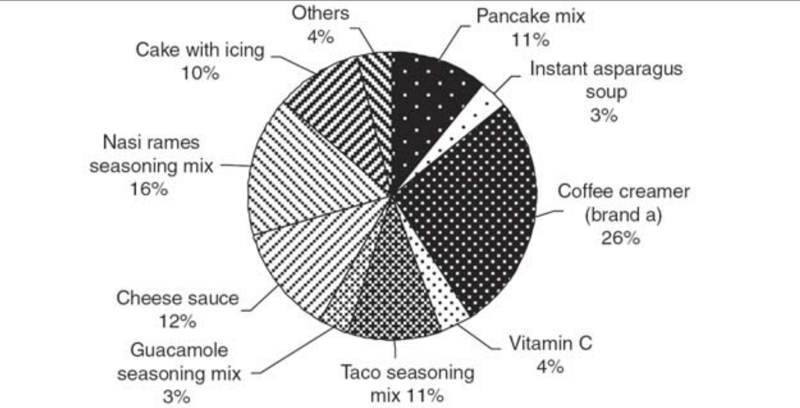

The results in the paper confirm that nanosilica is present in food products sold on the European market. The article also shows that nanosilica concentrations may change with food processing, although this was only considered for one food product (coffee creamer in hot coffee vs. water). Measured concentrations of nanomaterials are thus dependent on the sample preparation (e.g. sonification, temperature, solvent).

The study very well highlights the knowledge gaps and uncertainties in the different steps in performing a risk assessment of nanomaterials and points to priorities in research. In addition it may be mentioned that natural sources of silicon in food products were not considered in the calculation. The rather high limit of detection (0.3 mg/g; 1 mg/l) of the used analytical methods is a further limitation of the exposure estimation.

"Presence and risks of nanosilica in food products" ; S. Dekkers, P. Krystek, R.J.B. Peters, D.P.K. Lankveld, B.G.H. Bokkers, P.H. van Hoeven-Arentzen, H. Bouwmeester, A.G. Oomen : ***Nanotoxicology*** posted online on September 24, (2010).

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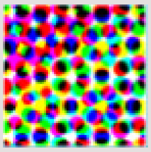

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