Safety assessment of nanoparticles and nanomaterials:

General aspects and the specific case of nanofibrillated cellulose

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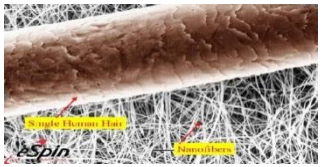
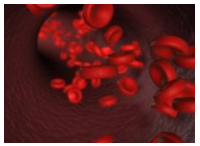
What are nanoparticles?

- Dimensions 0.1 µm or less (some scaling on the right)
- Specific properties:
  - High surface to volume ratio
- Enhanced surface activity

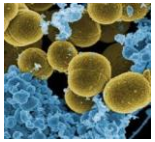
- Human hair, dimensions 25 – 250 µm



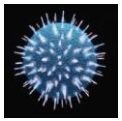
- Red blood cell, dimensions 10 µm



- A typical bacterium, dimensions 1 -3 µm



- A virus, dimensions tens to hundreds of nm



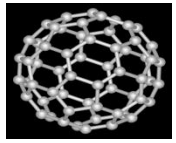
Examples of nanoparticles

Inorganic

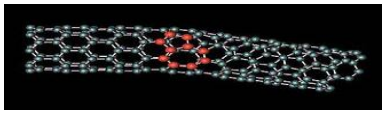
- Metals and their oxides
  - Nanosilver
  - Nanogold
  - TiO_2, Fe_2O_3, Al_2O_3, ZrO_2
  - Etc
- Minerals
  - Nanoclay
  - Silicates, including asbestos

Organic

- Carbon black
- Fullerens



- Carbon nanotubes



- Nanofibrillated cellulose (NFC)
- Atmosphaeric fine particles
- Wood dust

What makes nanoparticles special ?

- The specific surface properties mean novel catalytic and technological characteristics:
  - Altered optical properties
  - Enhanced ability to form suspensions and overcome problems caused by the density and viscosity of the solvent
  - Quantum level phenomena become significant alowing specific potential applications in electronics
  - Composites containing nanoparticles often have superior technological properties, such as increased durability
  - Etc.…

- Luster in pottery and glassware is an ancient example of altered optical poperties of nanometals and -minerals

Nanomaterials and safety

- The potentials are great, but are there risks?

How to assess risks?

- The (somewhat simplified) ”risk equation” is: Risk = Hazard x Probability
- The risk assessment start with hazard identification and characterization
- The hazards associated with nanoparticles, and specifically with nanofibrillated cellulose (NFC) are the specific topic of this talk

Factors that could make nanoparticles hazardous

General

- Potential to penetrate different biological barriers (gastointestinal barrier, blood-brain barrier, lung epithelium, skin etc)

Specific

- Toxicity of the material itself and its metabolic fate
- Size and shape of the nanoparticles (stiff, needle-like particles often more harmful than sphaerical ones)
- Potential to induce the formation of hazardous products; reactive oxygen species (ROS) a common example

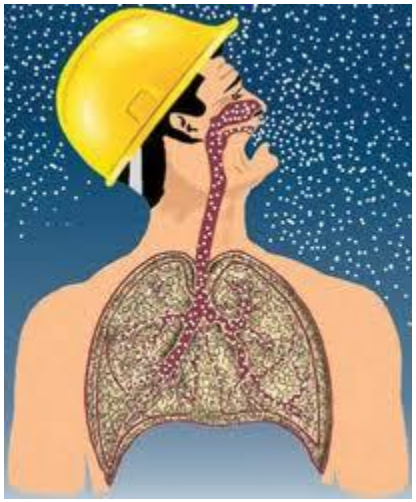
Examples of nanoparticle –associated harmful effects

Organic nanoparticles

- The association of atmosphaeric fine particles with cancer, respiratory problems and cardiovascular disease
- The occupational hazards of wood dust

Inorganic nanoparticles

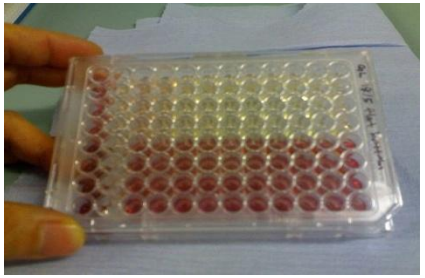
- Silicates are known as occupational hazards



How to characterize the hazards?

In vitro

- Cytotoxicity tests (ability to kill or damage cultured cells)
- Tests on the immune response of cultured immunologically active cells
- Genotoxicity tests (genotoxicity = the ability to damage DNA or chromosomes)



In vivo

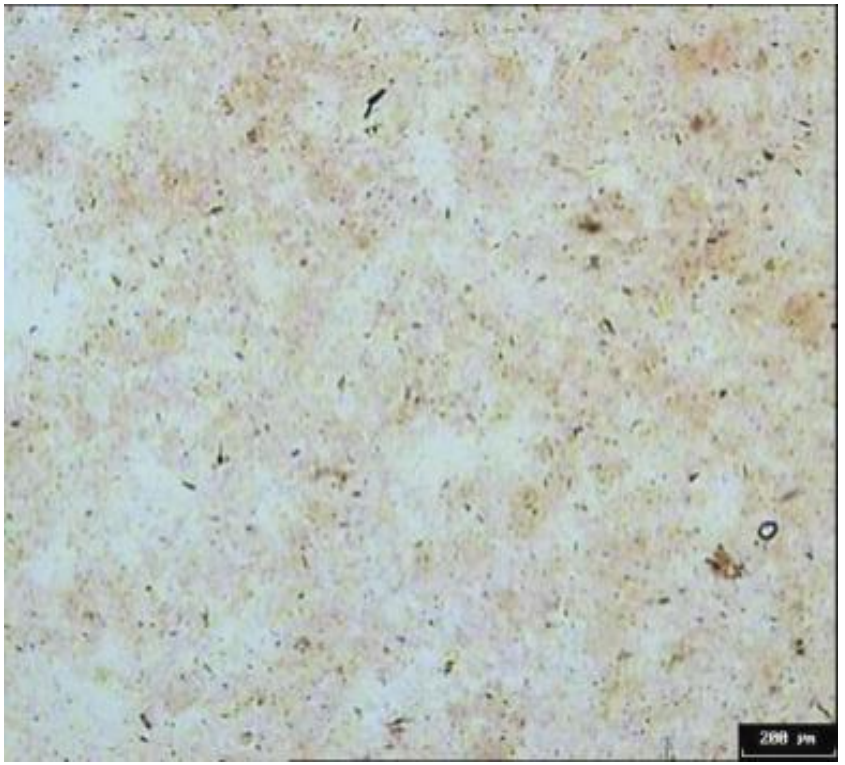
- Acute toxicity in experimental animals (oral, dermal or inhalatory)
- Repated dose toxicity tests (28- or 90-day tests)
- Chronic toxicity tests (up to two years in rodents)
- Tests on reproductive toxicity (multigeneration studies)
- Others…

An example: Tests proposed by the European Food Safety Authority (EFSA) for nanomaterials present in food or feed

- If engineered nanomaterials will be present in the final food or feed matrix, a set of toxicological tests is recommended (EFSA Journal 2011;9(5):2140 [36 pp.])
  - In vitro genotoxicity tests
  - Repeated dose 90-day oral toxicity study in rodents
  - *In vitro* digestion studies
  - If necessary other *in vitro* studies
  - If necessary developmental toxicity studies, *in vivo* genotoxicity studies, chronic toxicity studies, specific toxicity tests etc

NFC – Any Potential Hazards ?

- Cellulose is inert in human body (however, microcrystalline cellulose is an accepted food additive E460)
- Because of the fibrillous nature, NFC could in certain respects resemble mineral fibres
- The dimension could allow the NFC to reach the lungs by inhalation
- Possibility to induce the formation of ROS



The SUNPAP project and NFC-safety

- A specific Module (Module 4) has been devoted to hazard identification and characterization and subsequent risk assessment taking into account the potential exposure scenarios
- Both extensive in vitro testing and targeted in vivo testing have been applied to the selected representative NFCs
- The outcome of the toxicological studies and the actual risk assessment will be summarized in separate presentations on Wednesday, 20th June 2012 :
  - 12.05-12.30 Nanofibrillated cellulose: Results of in vitro and in vivo toxicological assays (*Hannu Norppa, FIOH)*
  - 14.20-14.45 Risk assessment of nanofibrillated cellulose in occupational settings (*Juulia Rouhiainen, Pöyry)*

Acknowledgement

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