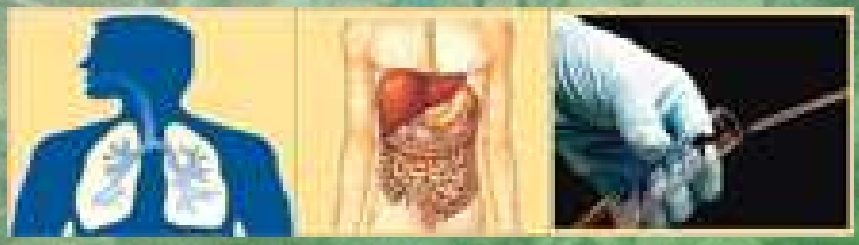
European Strategy for Nanosafety

nanoSAFE

Safe production and use of nanomaterials

What is nanotoxicology?



How to estimate the potential hazard related to nanoparticles?

Dissemination report
October 2008
DR-225 200810-5

Project ID NMP2-CT-2005-515843

An European Integrated Project Supported by through the Sixth Framework Programme if research and Technological Development

Dissemination reports from Nanosafe2 project are designed to highlight and present in a simplified way the main results obtained in the studies carried out during this project. These reports mainly deal with one question which is of general concern for whom is interested by the safe production and use of nanomaterials. The full results are summarized in the corresponding Technical reports.
***All the Dissemination reports and Technical reports are publicly available from Nanosafe2 project website**: http://www.nanosafe.org*

Refer to:

***D225:** Report on pharmacokinetics in vivo and in vitro*

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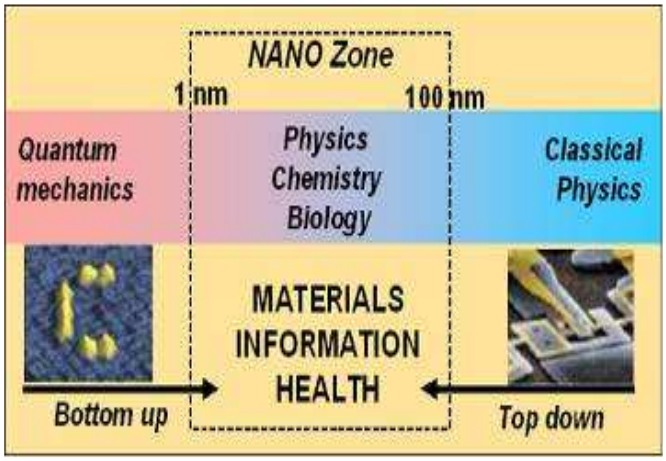
Is the toxicity of nanomaterials different compared to larger materials or chemical toxicity?

Toxicology is the science that describes the negative health effect of exposure to chemical substances or physical agents, in environmental, occupational, or therapeutic setting.



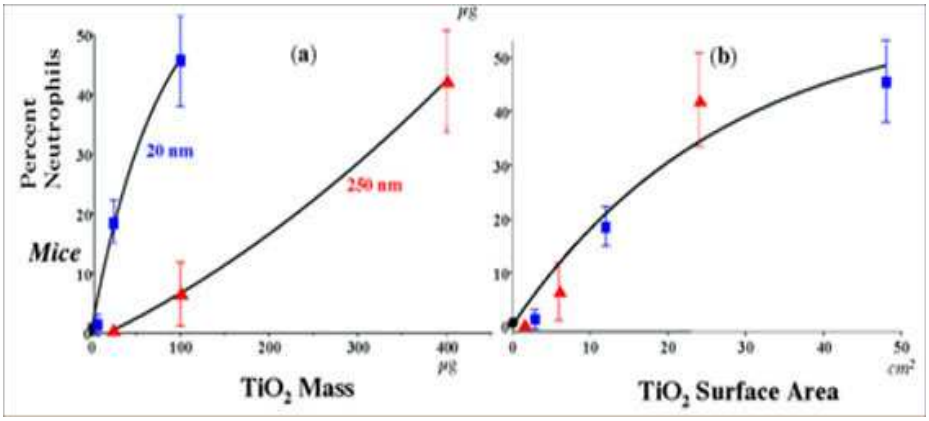
Two convergent and complementary approaches of the "nano"zone.

Nanomaterials and particles are pieces of matter in the size range of 1–100 nm in one or more dimensions. Thus significant smaller than micrometer-sized particles and yet larger than atoms and various molecules. Typically in this size range, material has to some extent special physical and chemical properties. That is actually why nanomaterials are produced, but as a consequence we cannot predict simply their (toxic) biological effects on the basis of their chemical composition alone.

One of the results that arise from research studies is that on a mass basis (that is, per kg for example), the toxicity of nanomaterials is often enhanced compared to that of larger micrometric Particles.

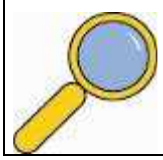
It seems that increased toxicity is related to the increase in total surface area offered by nanoparticles (that is also linked to their increased catalytic power).

Lung inflammatory reaction after respiratory exposure of mouse to nanoparticles of 20 and 250nm



***Mass dose**: the reaction is more important for the particles of 20nm*
***Surface area dose**: the reaction is equivalent for two types of particles (Oberdoster Oct 2004)*

However, there are significant deviations from that rule; the reasons for these differences are currently poorly understood but it is increasingly clear that not only size but also surface charge, reactivity, shape, solubility, impurities present in the final product etc*. play a role in explaining the activity and toxicity of nanomaterials.*



The study of toxic effects of nanomaterials is still under development and many questions are unanswered.

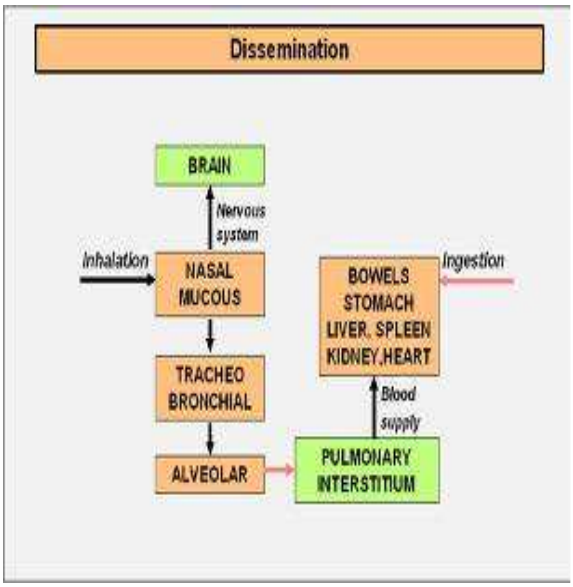
How are we exposed to nanomaterials?

Nanoparticles can be present in air, food, water, cosmetics, or drugs. There are three natural routes via which a substance can enter a human body, namely through the ***skin****, or after* ***ingestion*** *or* ***inhalation****. In any case contact will be necessary.*
.When ingested most nanoparticles are rapidly eliminated via the feces; however some may be taken up by the gut and distributed to the other organs.

Some studies suggest that nanoparticles also can enter the body through the skin, especially during occupational exposure (effect of flexing – rubbing).

Some recent studies indicate that nanoparticles of titanium dioxide (TiO2) used in sunscreens do not penetrate beyond the epidermis. Yet, it has also been reported that nanoparticles with varying physicochemical properties (size less than 20 nm) were able to penetrate the intact skin of pigs, depending on size, shape, and surface coating.

Inhalation *is considered to be the most troublesome route of exposure.*
The deposition of discrete nanoparticles in the respiratory tract is determined by the particle size (aerodynamic diameter). We also know that nanoparticles in the lungs can be transported to other organs in the body, although it is not well known how this is influenced by the chemical and physical properties of the nanoparticles.
Beside a possible effect on different target organs, inhaled nanoparticles can have a local effect in lung. Studies in lungs of rats have shown that ultrafine, nanometric, particles induce more inflammation and are more tumorigenic than an equal mass of larger particles.



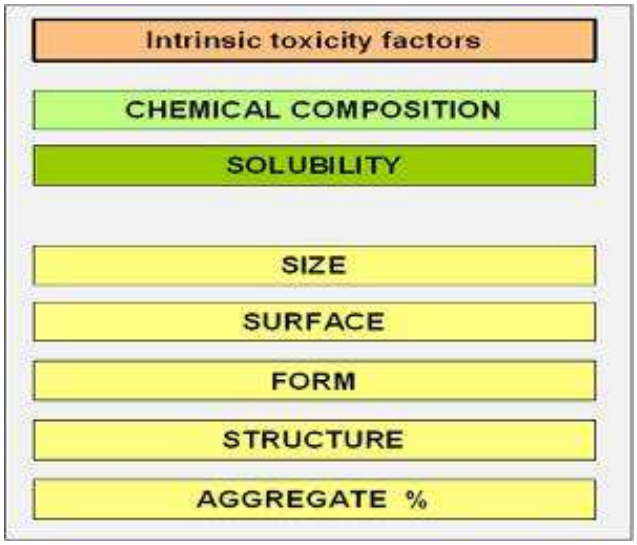
Dispersion route in case of inhalation exposure

Nanoproducts'number grows very rapidly. It is therefore urgent to assess for each of them the likely routes of exposure and the potential toxicity.

Which issues are important in nanotoxicology?

The most critical issues in evaluating the toxicity of nanomaterials are:

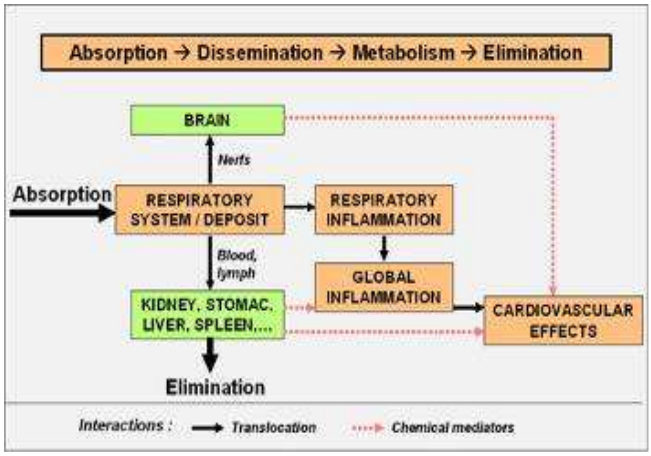
- *To be able to explain and understand the toxicity of a nanomaterial a **detailed description** – characterization - of the material is needed. Moreover, a thorough description of the coating (with a variety of oxides, oxy-hydrates, organic compounds, and surfactant) and possible impurities must also be provided.*
- *In particular, size, crystal form, size distribution, shape, agglomeration state, chemical composition, surface area and surface charge are parameters to consider for all nanomaterials.*

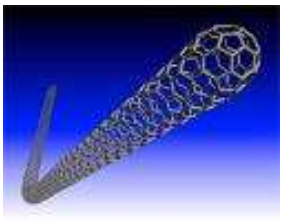


Nanotoxicity Factors

- *The production of **oxidants**, either directly on the surface of the material or due to the interaction with a biological entity, is a common observation for almost all nanomaterials.*

- *Although we know that nanoparticles are able to translocate from one organ of the body to another, the body distribution (toxicokinetics) of different types of nanomaterials is not well studied and even less understood.*
- *Fibrous nanomaterials deserve special attention because the comparison with asbestos is an important issue, undoubtedly so since the parution of two publications by Poland et al. (2008) and Takaii et al. (2008). Those authors show that in some mice, multiwall carbon nanotubes induced pathology in the mesothelial lining of the body cavity (related to the chest mesothelial lining, target tissue of asbestos cancer effect). Wick and colleagues (2007) found that single wall carbon nanotubes agglomerates and asbestos had similar effects on cell survival and proliferation in a human mesothelioma cell line cultured in test tubes.*





Nano tube simple wall

Abestos fiber

More research is needed to better understand specific particle properties and other factors that influence their toxicity

What studies are urgently needed?

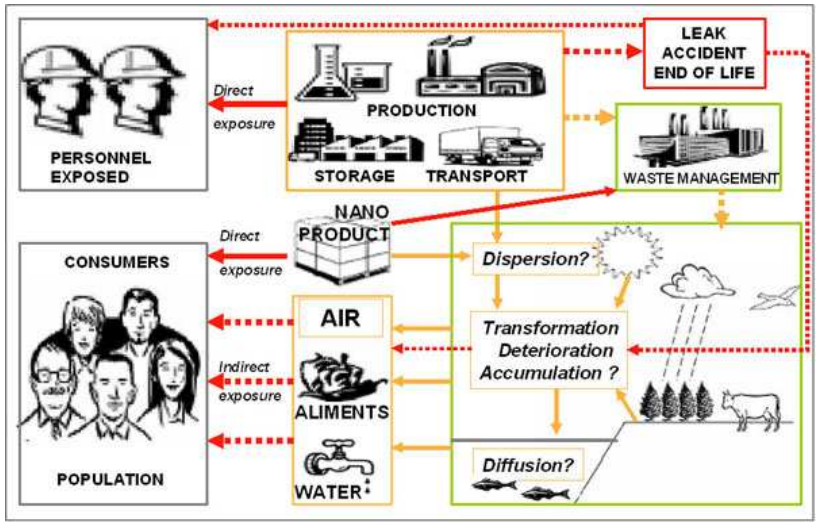
As each particle type should be tested individually, the development and validation of methods to evaluate the toxicity of engineered nanomaterials are required.

Chips replace mices! *Highly parallel cell culture in nanodrops, a new format for high content toxicology cell based assays. TOXDROP, Béatrice SCHAACK, NANOBIO*

*As written by Sayes 2007: "It seems clear that in **vitro cellular systems** will need to be further developed, standardized, and validated (relative to in vivo effects) in order to provide useful screening data on the relative toxicity of inhaled particle types(Sayes et al., 2007)".*

*Not only do we need to evaluate the toxicity of different materials but we also need to predict, with a relatively simple test battery, the **potential impact** of engineered nanomaterials **on the environment and human health.***

*In that evaluation, we should consider the possible health impact of engineered nanomaterials over their **entire life-span**.*

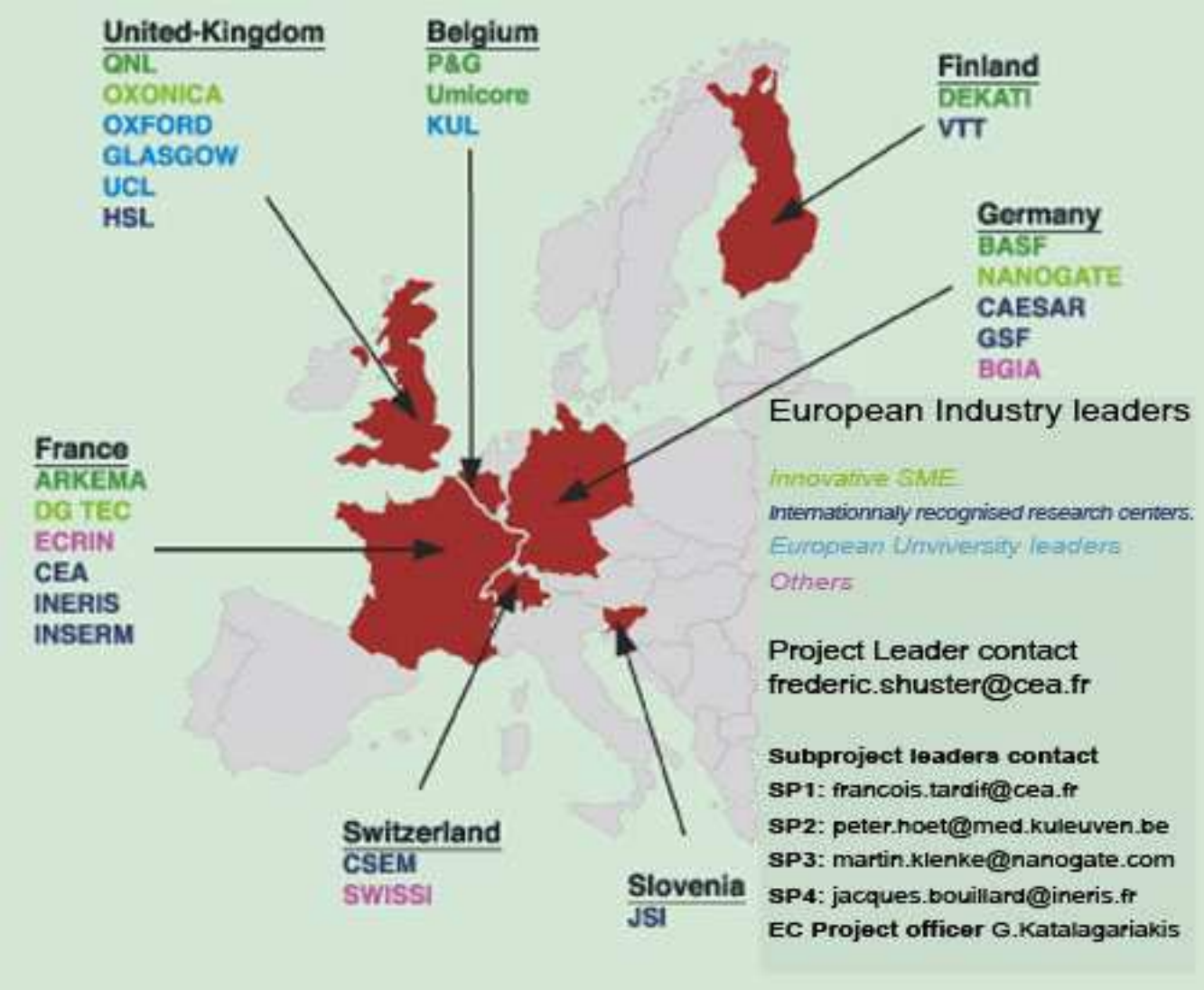


Global life cycle: direct or indirect exposure critical phases

New toxicity methods have to be developed and validated.
Potential impact on human health and environment should be tested over the entire life-span of the material.

Nanosafe2 brings together twenty five partners from seven countries of the European Union, mainly small, medium and large enterprises and public research laboratories. The project is supported through the Sixth Framework Programme for Research and technological Development of the European Commission and addresses the thematic priority3.43.2-1: Hazard reduction in production plant and storage sites. The project started in April 2005 and will end in March 2009.
Nanosafe2 main objective is to develop risk assessment and management for secure industrial production of nanoparticles. It focuses on four areas: detection and characterisation techniques, Health hazard assessment, development of secure industrial production systems and safe applications, societal and environmental aspects.

Partners



http://nanosafe.org
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- ***More research is needed to better understand specific particle properties and other factors that influence their toxicity.***
- ***New toxicity methods have to be developed and validated.***
  Potential impact on human health and environment should be tested over the entire life-span of the material.

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http:/www.nanosafe.org