Finnish Institute of Occupational Health

SAFETY OF ENGINEERED NANOPARTICLES AT WORKPLACES

Kai Savolainen

NATO Workshop
Nanomaterials: Environmental Risks and Benefits and Emerging Consumer Products
Faro, Portugal, April 27-30, 2008

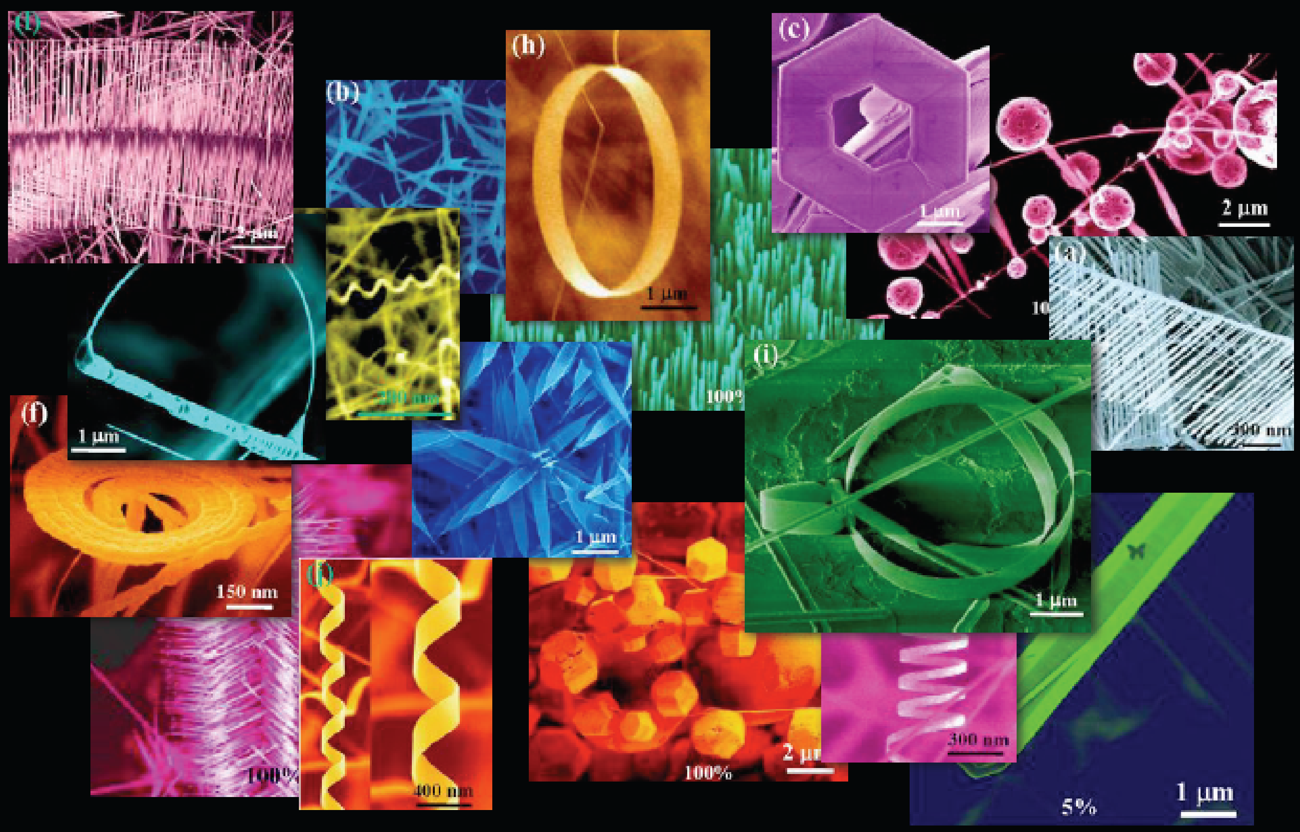
Contents of the presentation

- Introduction
- Characterization of and assessment of exposure to engineered nanoparticles (ENP) at workplaces
- Experimental exposures
- Pulmonary inflammation
- Genotoxicity
- ENP at workplaces – workers at risk?
- Challenges to assure workplace safety and conclusions

Outlook and scope of nanotechnologies

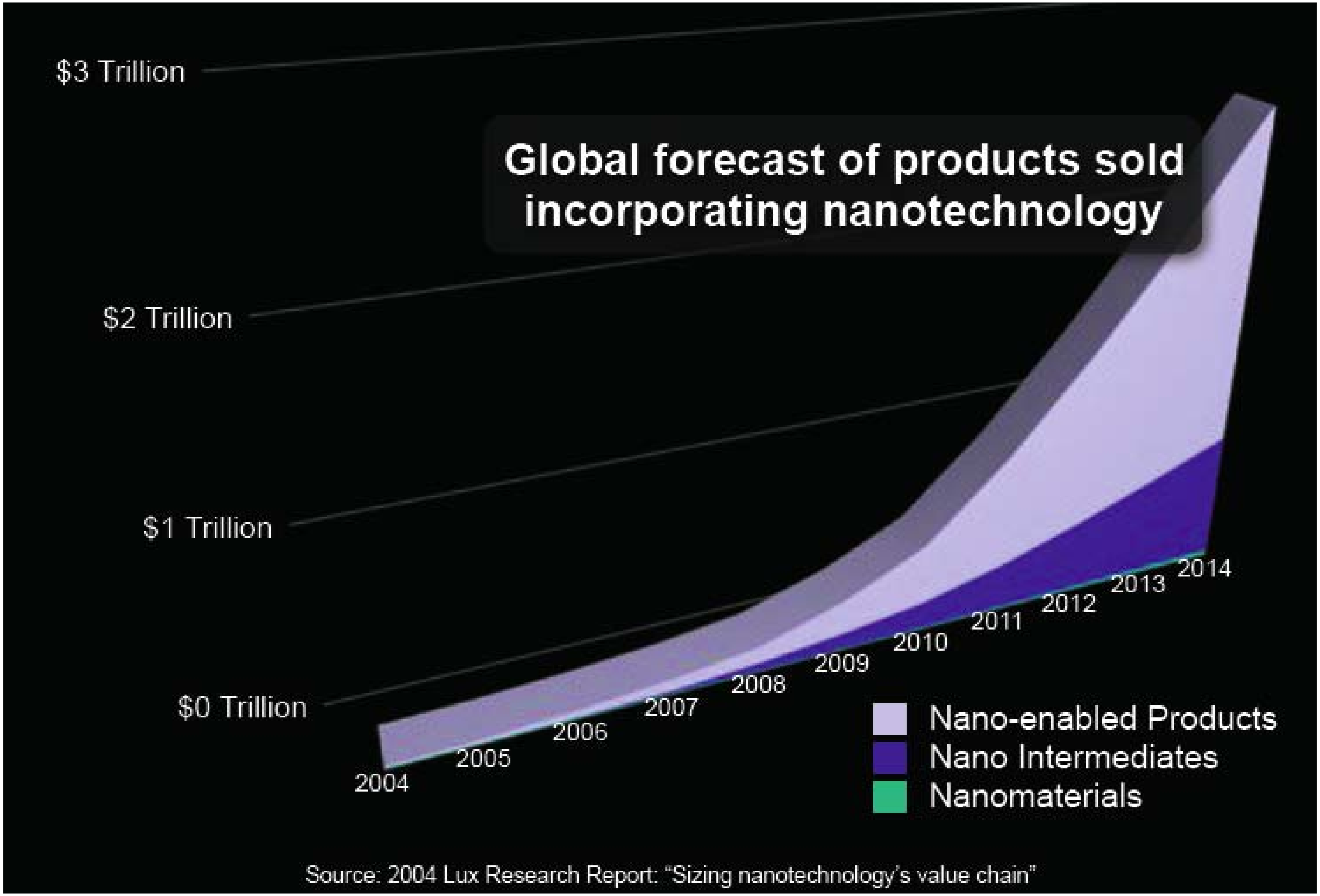
- At the beginning of the next technological revolution
- New materials, properties products and processes
- Massive investment by governments and industry
- Huge impact for the economy and society
- Potentially marked impact on the health of workers and consumers

New diversity: Threat or opportunity?



Nano-ZnO: One chemistry, many shapes
Courtesy of Prof. Z.L. Wang, Georgia Tech

Economic Benefits of Nanotechnology



Quality of life and social benefits of nanotechnology

From Andrew Maynard, Chief scientist of The Project on Emerging Nanotechnologies

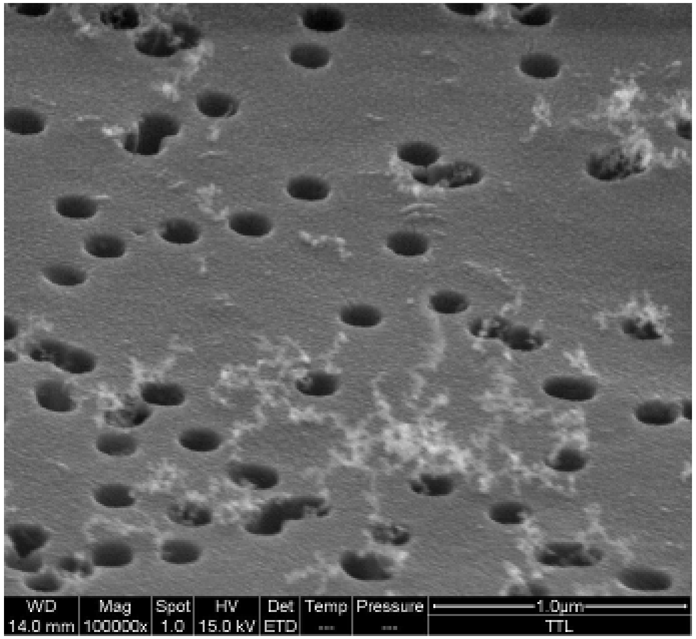
Nanotechnology safety concerns – special emphasis on workplaces

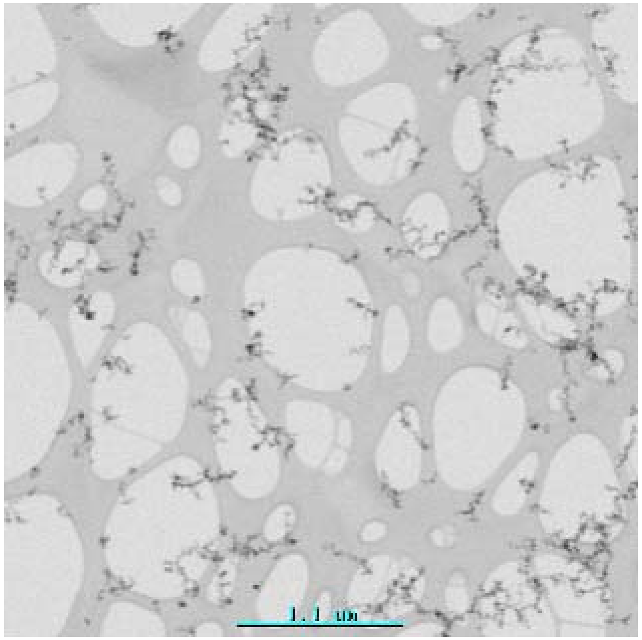
Risks and safety

- **Human health and safety**
  - Potential health effects especially for workers due to higher exposure levels, but also to consumers
  - Very little known about the health risks of ENP
  - Levels of exposure to ENP are unknown due to lack of user-friendly measurement devices
- **Environmental contamination**
  - Behavior of ENP in the environment
  - Exposure of the environment to ENP, and humans via the environment
  - Effects of ENP in organisms in the environment

Synthesis and characterization of ENP: Nanoparticles synthesized for toxicity tests

- TiO2 ENP synthesized by vaporizing titanium tetraisopropoxide (TTIP) and thermal modifying. TTIP is decomposed in the reactor and TiO_2 agglomerates are produced and collected onto filters and TEM-grids for EM to define the shape and composition of nanoparticles and agglomerates.



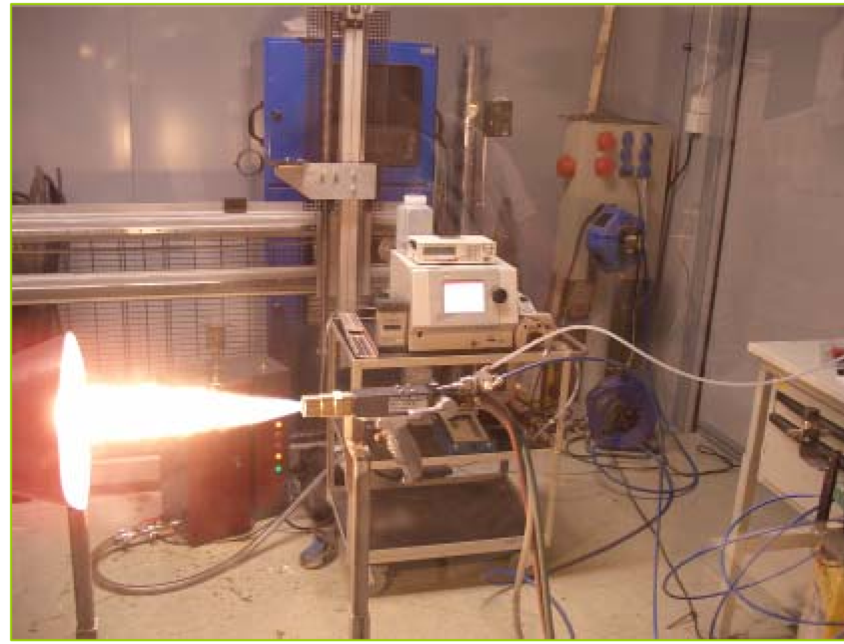


TiO_2 samples on micropore filter (left) and on carbon film supported TEM grid (right).

Vippola et al, unpublished

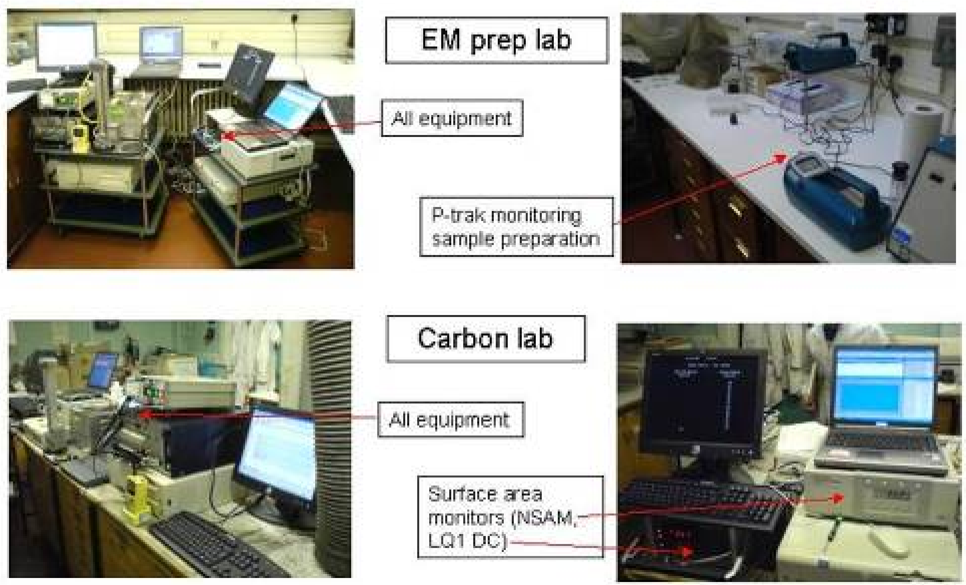
Synthesis and characterization: Preparation of ENP by liquid flame spray (LFS) method

In the LFS process, the liquid precursor is atomized into micro-droplets introduced into a turbulent H_2–O_2 flame. Evaporation of the liquid droplets in the flame, followed by decomposition and re-condensation, generates a well-defined, nearly mono-dispersed ENP to be sprayed on a surface or to be collected.



From Vippola with permission

Exposure assessment: Instruments required on-site – nano laboratories



Instruments used in two nanotechnology laboratories in a university

With permission of Dave Mark

Instruments required for:

❖ Number size distribution:	*Scanning Mobility Particle Sizer*
❖ Number concentrations:	*Condensation Particle Counters*
❖ Surface area concentrations:	*Diffusion Charger Monitors*
❖ Mass concentrations:	*Piezo-balance or Low Pressure Impactors*
❖ Particle collection for characterisation:	*Electrostatic or thermal precipitator deposit on TEM grids and polycarbonate filters for use in personal sampling heads*

Exposure assessment: Instruments required on-site – powder handling

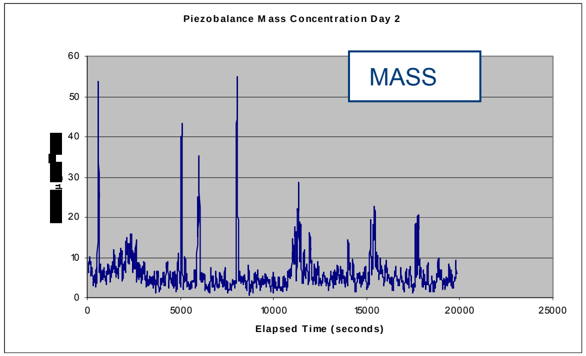
Instruments used when sucking powder out of bin at TiO_2 production and bagging plant

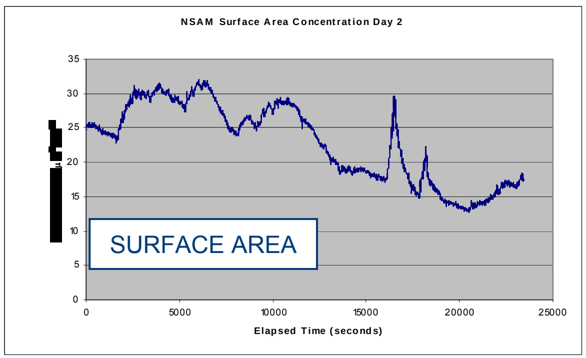
With permission of Dave Mark

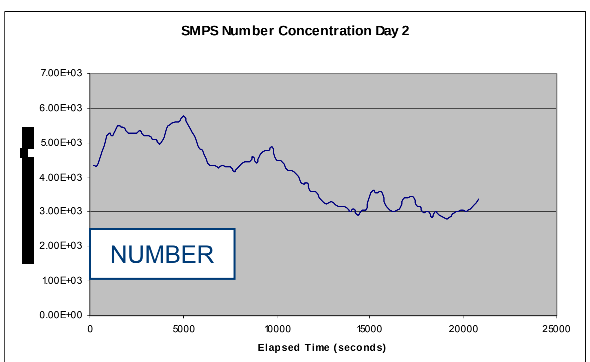
Instruments required for:

- Number size distribution: *Scanning Mobility Particle Sizer*
- Number concentrations: *Condensation Particle Counters*
- Surface area concentrations: *Diffusion Charger Monitors*
- Mass concentrations: *Low Pressure Impactor + standard respirable dust filter samplers*
- Particle collection: *Electrostatic precipitator deposit on TEM grids*

Exposure to ENP in a university nano laboratory







- Monitors are run continuously throughout the day
- Activities are then superimposed on the record
- Levels from one university

Mass: 6 – 11 µg m^{-3}

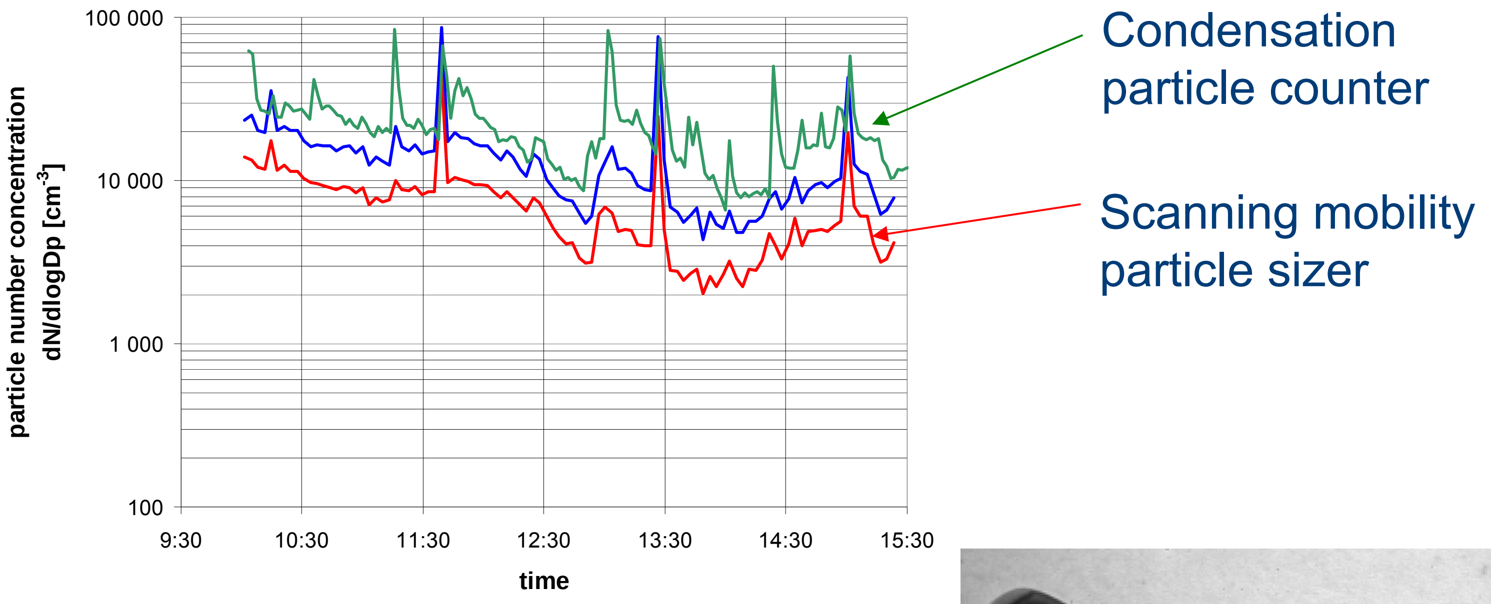
Number: 4 – 500 x 10^3 particles cm^{-3}

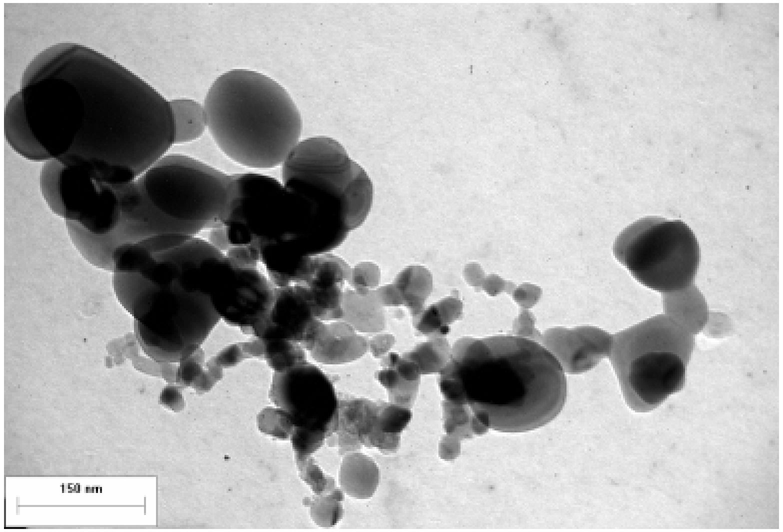
Surface Area: 45 – 110 μm^2 cm^{-3}

Number median diameter: 39 – 58 nm

Mark et al, unpublished

Exposure to ENP: Sucking TiO_2 powder of drum

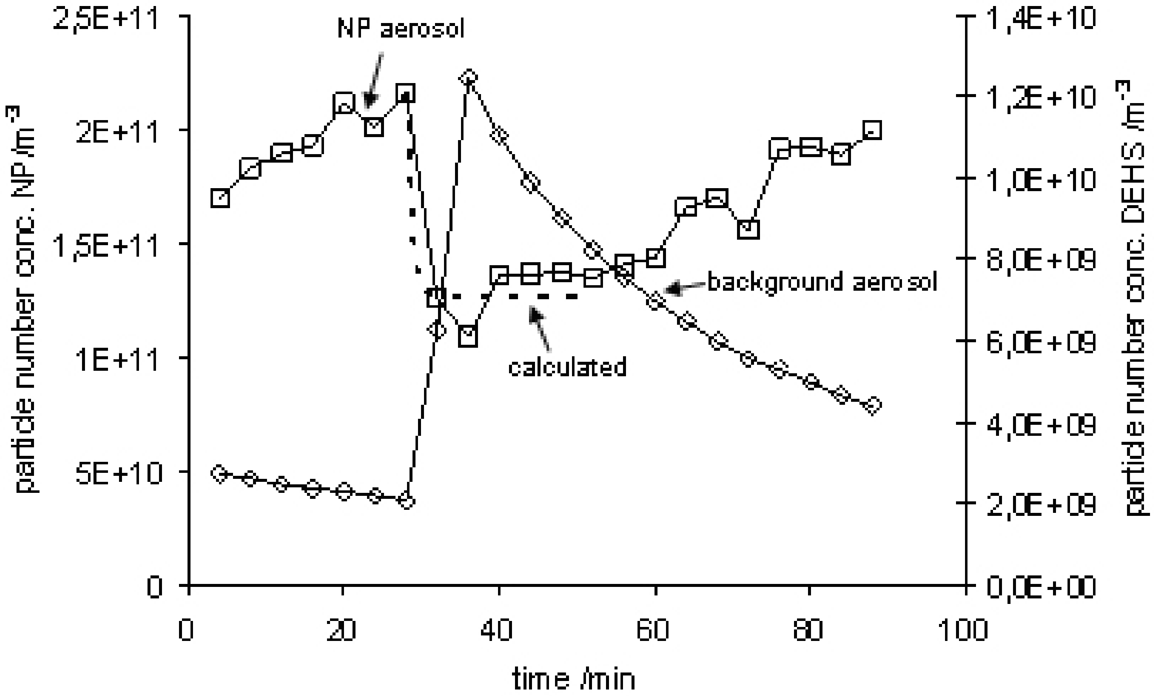




TEM photograph of TiO_2 particles collected on electrostatic precipitator

Mark et al, unpublished

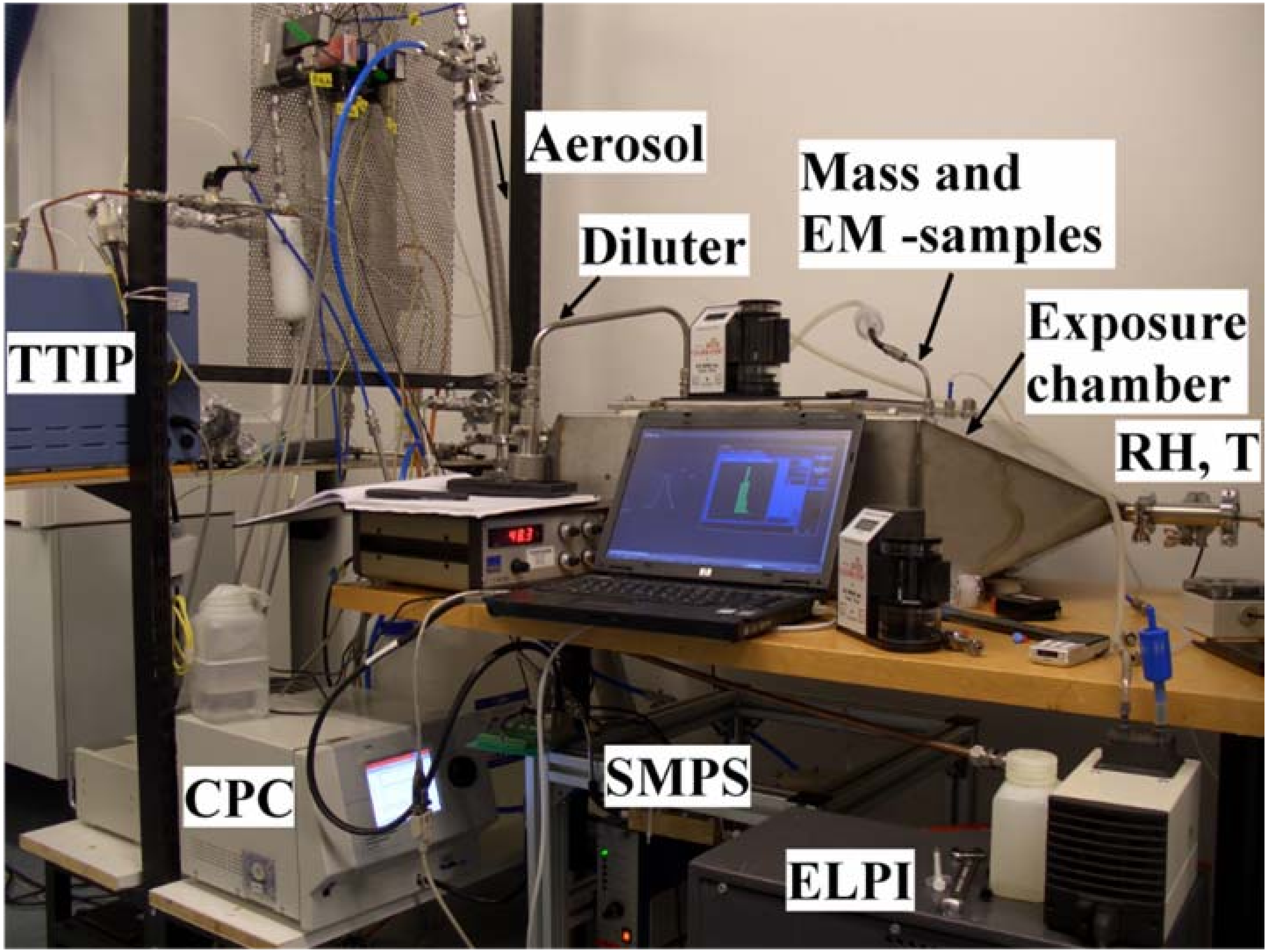
Behavior in Platinum ENP concentrations in the presence of background aerosol



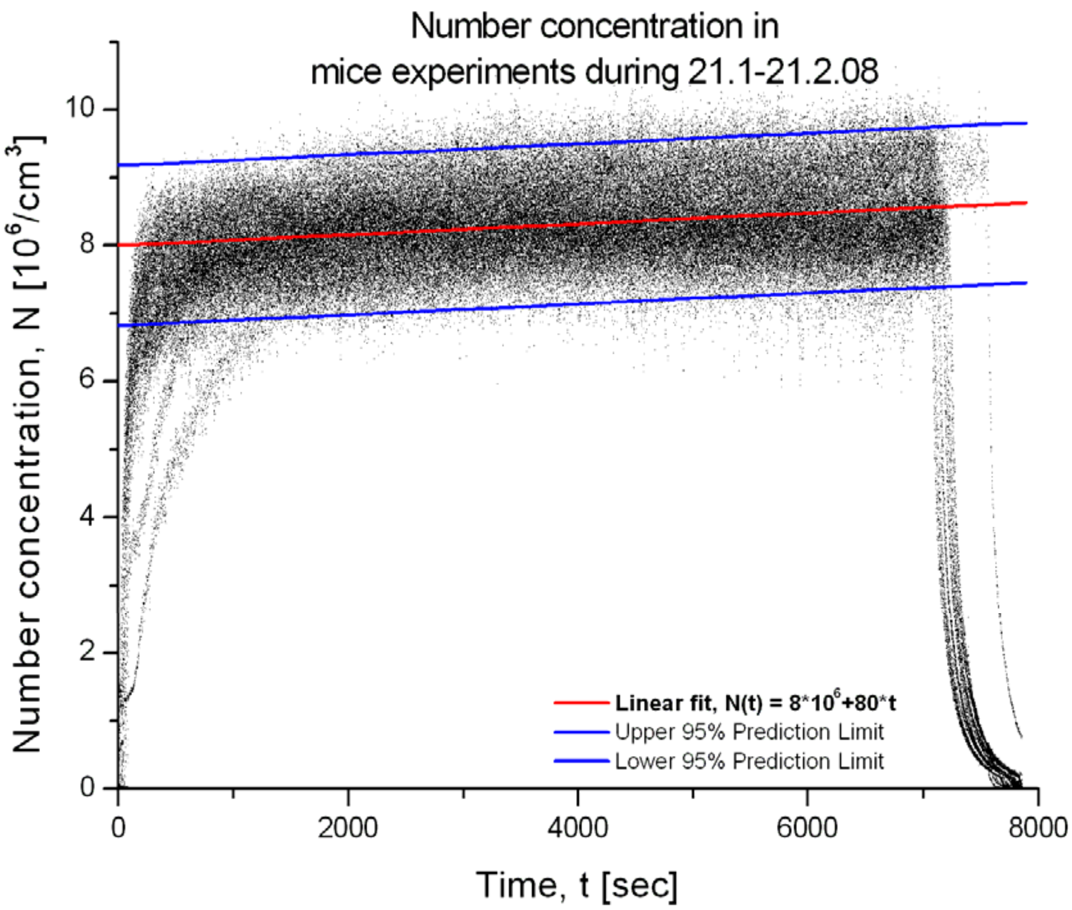
- Background aerosols decrease the levels of primary aerosols through coagulation; **Source**: M. Seipenbush, A Binder, G. Kasper. Experimental Report and Conclusions of NANOTRANSPORT project, 2008, preliminary draft

Reaction of the concentration of the NP aerosol to a rapid change in the background concentration: no delay visible on the experimental timescale

Experimental exposures: *In vivo* exposure set-up



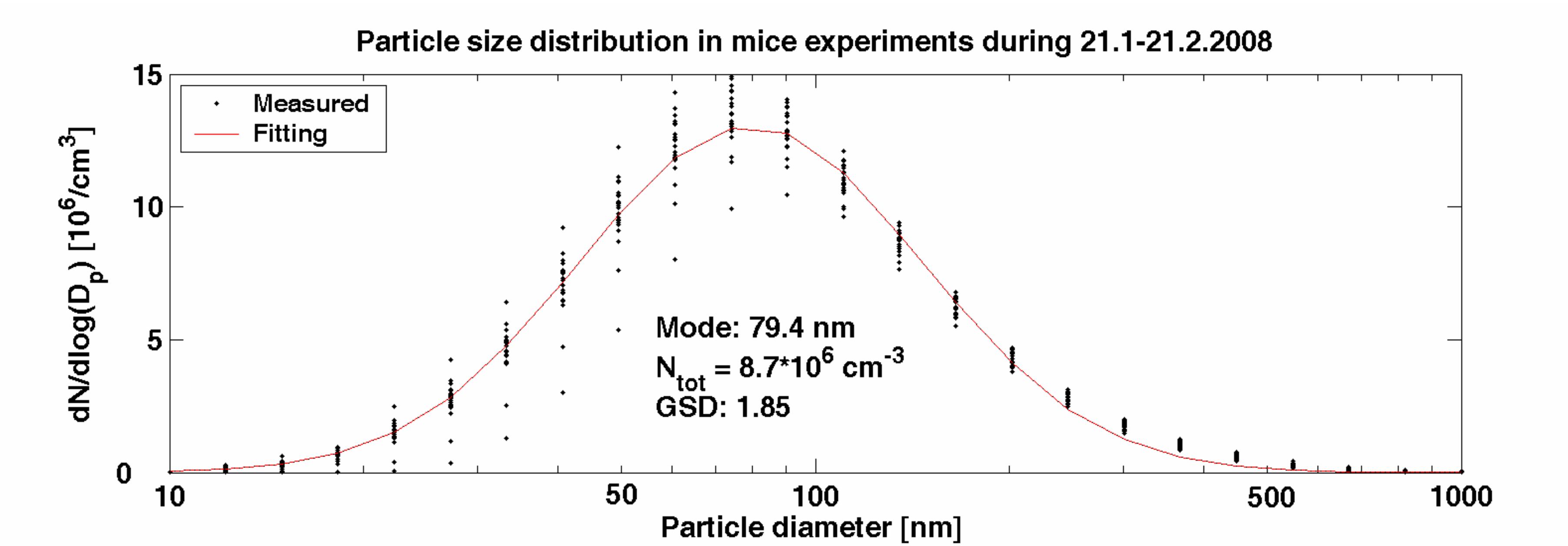
TiO2 number concentrations during *in vivo* exposures for pulmonary inflammation



Concentrations high as compared with occupational exposure

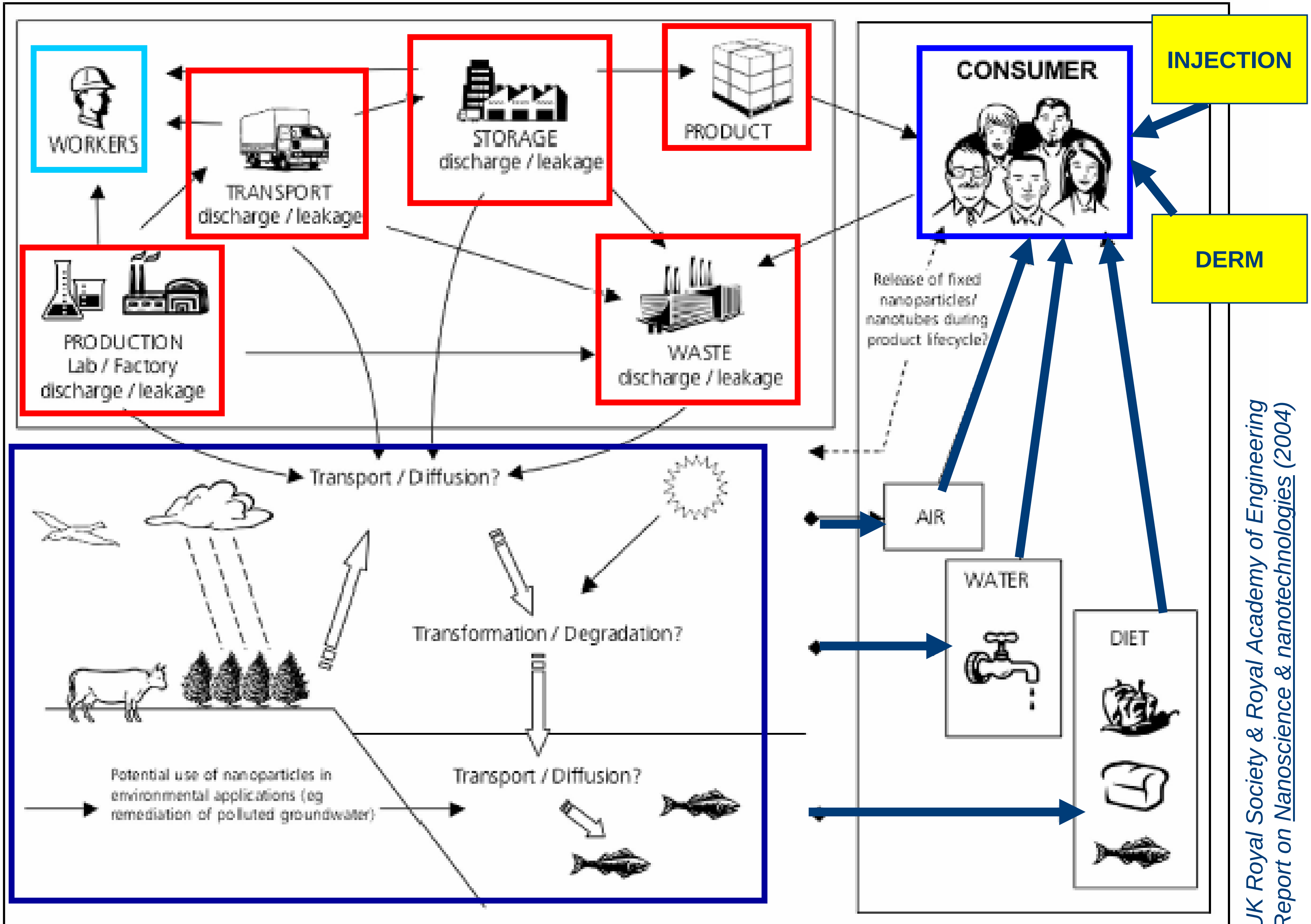
Koivisto and Hämeri, unpublished

Size distribution of TiO2 NP during *in vivo* exposures



Koivisto and Hämeri, unpublished

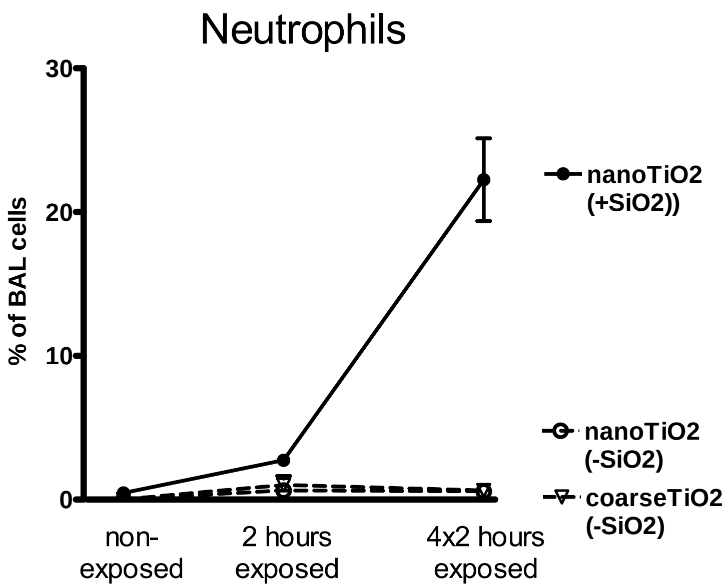
Exposure: sources, targets & routes



UK Royal Society & Royal Academy of Engineering
Report on Nanoscience & nanotechnologies (2004)

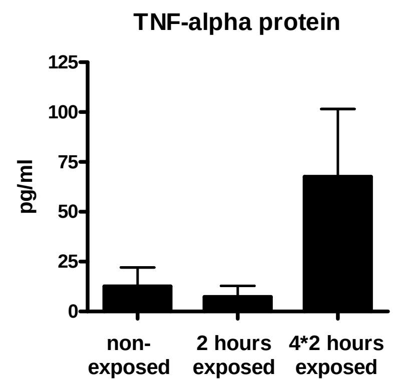
Pulmonary inflammation: Pulmonary neutrophilia and TNF-alpha secretion in mouse lungs and in RAW 264.7 macrophages

TIO2 exposed mice (BAL)

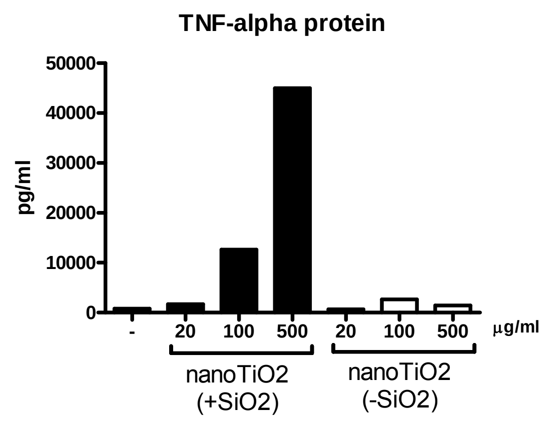


Alenius et al, unpublished

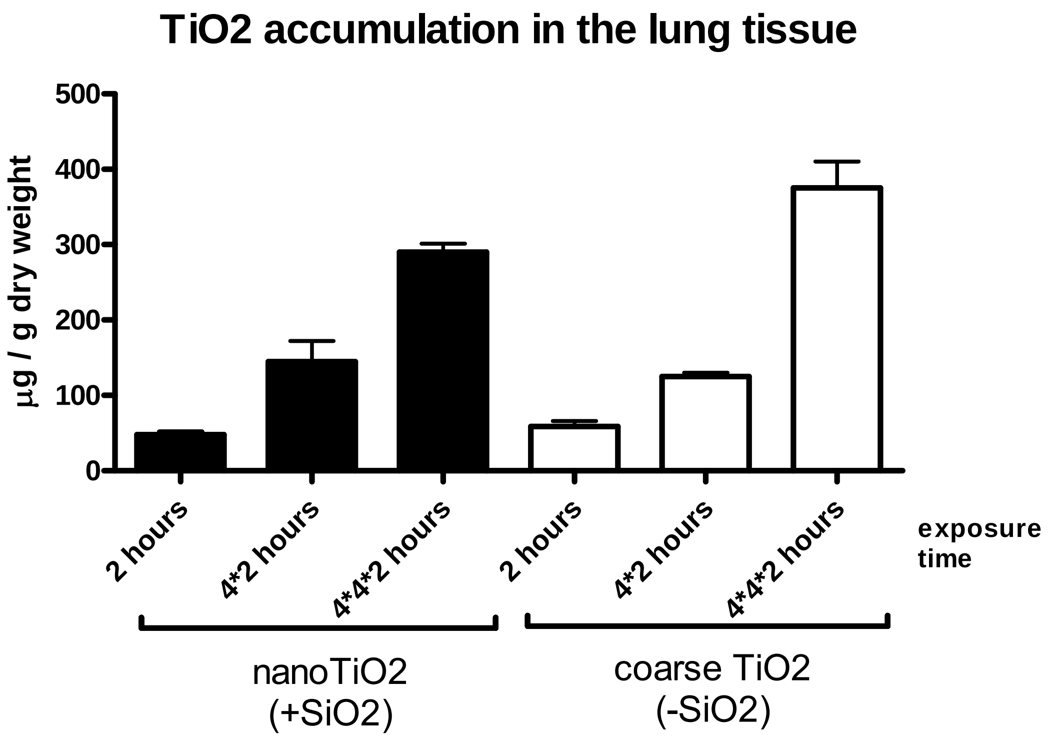
nanoTIO2 (+SiO2) exposed mice (BAL)

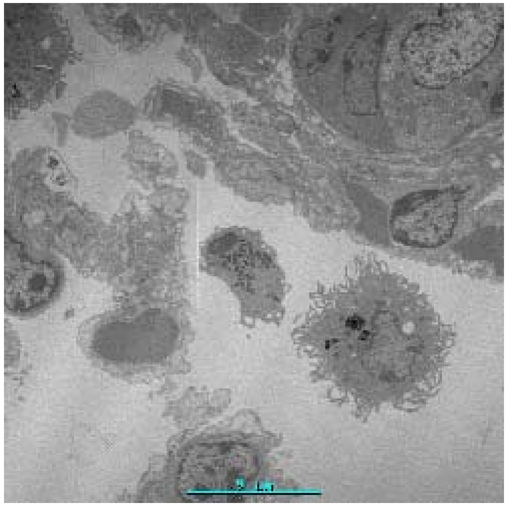


RAW 264.7 macrophages



Pulmonary inflammation: TiO2 accumulates in lung tissue and lung macrophages after inhalation exposure in mice

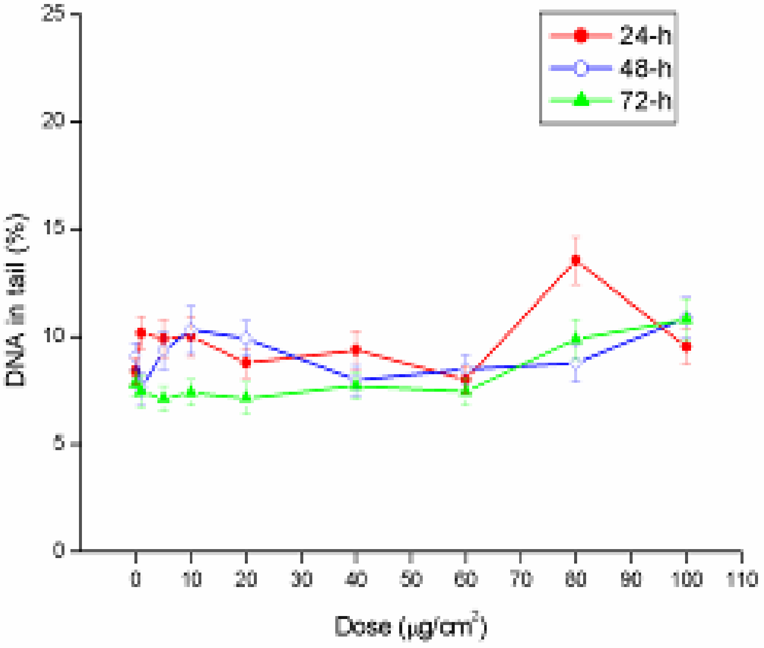




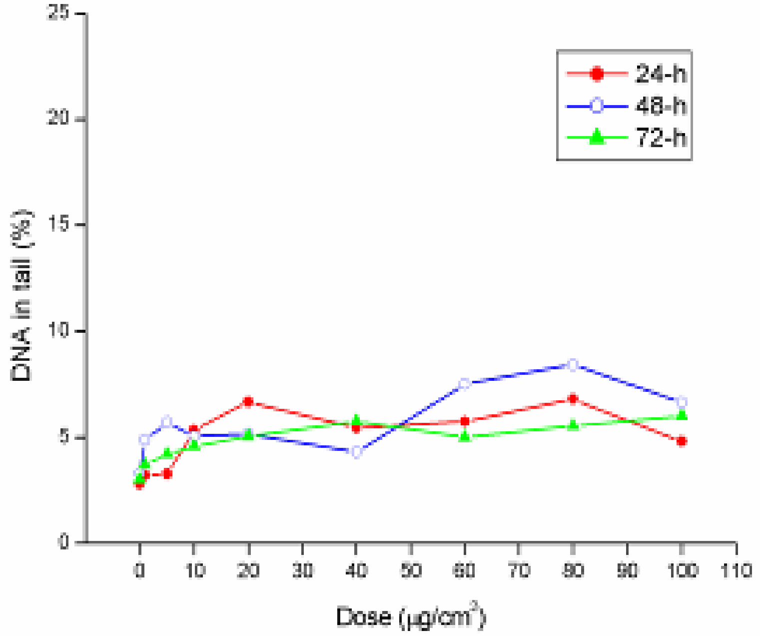
Alenius et al, unpublished

Genotoxicity of nano-sized titanium dioxide

- Human bronchial epithelial BEAS 2B cells *in vitro*
  - DNA damage (comet assay) induced by nano-sized anatase and rutile TiO_2 and fine rutile TiO_2



DNA damage induced by nano-sized TiO_2 rutile (SiO_2 coated) in human bronchial epithelial BEAS 2B cells



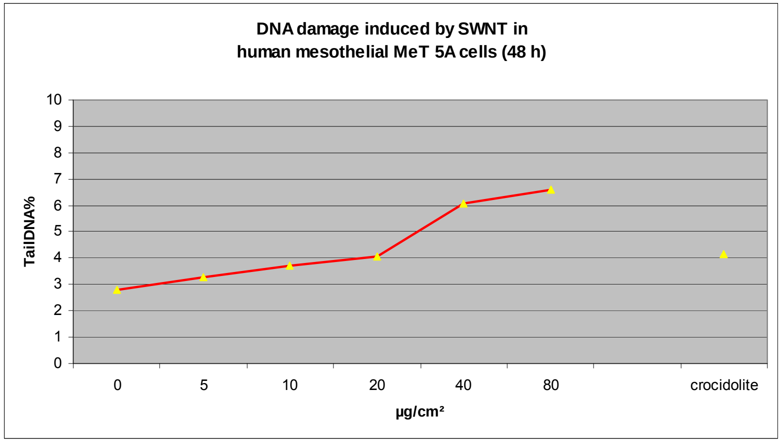
DNA damage induced by nano-sized TiO_2 anatase in human bronchial epithelial BEAS 2B cells

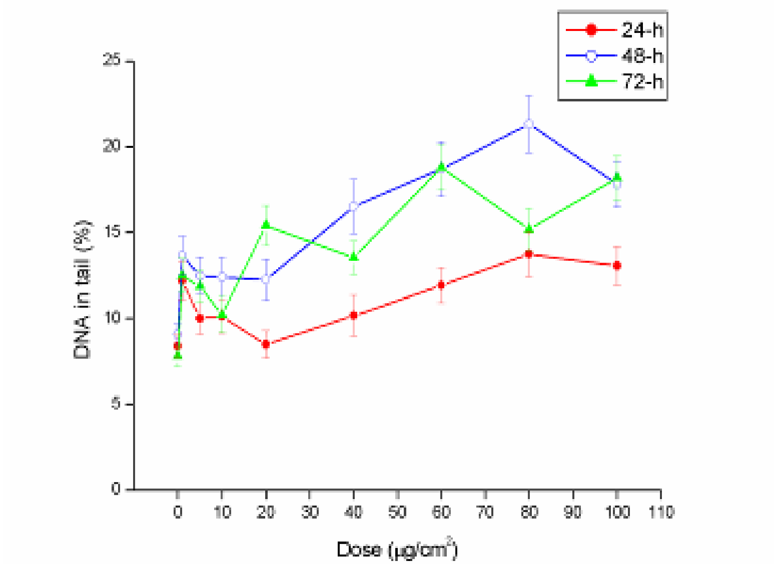
Norppa et al

Genotoxicity of carbon nanotubes

- Human mesothelial Met 5A cells *in vitro*
  - DNA damage (comet assay) induced by single-wall and multi-wall carbon nanotubes
- Human bronchial epithelial BEAS 2B cells *in vitro*
  - DNA damage induced by single-wall, multiwall and mixed carbon nanotubes
  - Micronuclei induced by mixed (>50% Single-wall) carbon nanotubes

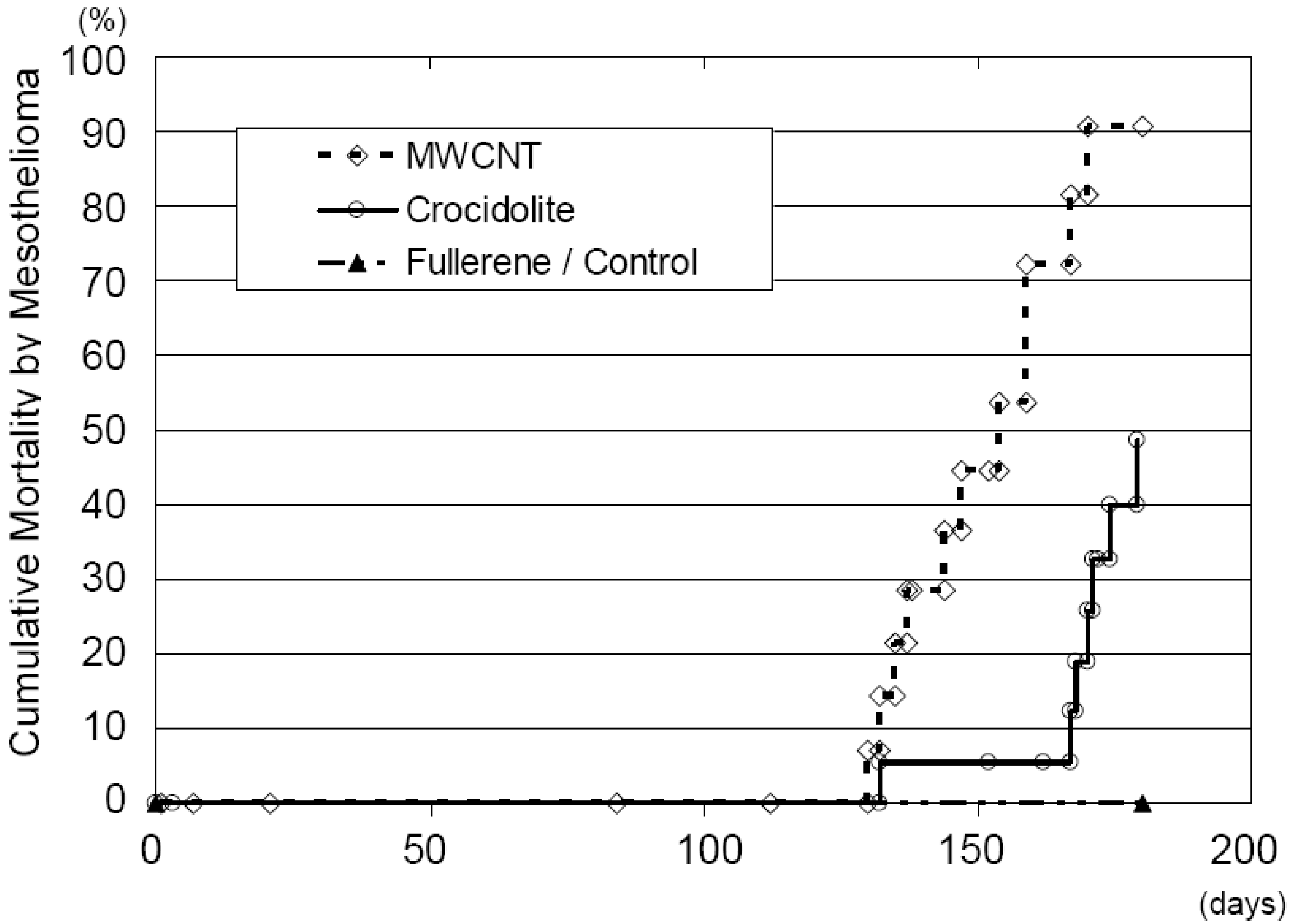
Norppa et al





DNA damage induced by carbon nanotubes (mixed SW and MW) in human bronchial epithelial BEAS 2B cells

MWCNT-induced mesotheliomas in a highly sensitive mouse-model



Takagi et al. Induction of mesothelioma in p53+/− mouse by intraperitoneal application of multi-wall carbon nanotube . The Journal of Toxicological Sciences (2008) 33:105-116.

ENP at workplaces – workers at risk?

- Need to know exposure levels to ENP at workplaces and to understand, manage and minimize potential risks of ENP in workplaces and beyond
- Need to take an action to allow assuring a safe workplace for workers potentially exposed to ENP:
  - agreement on appropriate metrics to define dose and exposure
  - easy-to-use devices for exposure assessment
  - separation of ENP from the background NP
  - translocation of ENP into and in the body; identification of target organs such as brain, liver, kidney and lungs
  - toxicity mechanisms of ENP and their determinants
  - model and extrapolate exposure and effects
- What if we get it wrong – unpleasant surprises in workplaces, in the production of ENP or in ENP consumer applications

Nanosafety information needs

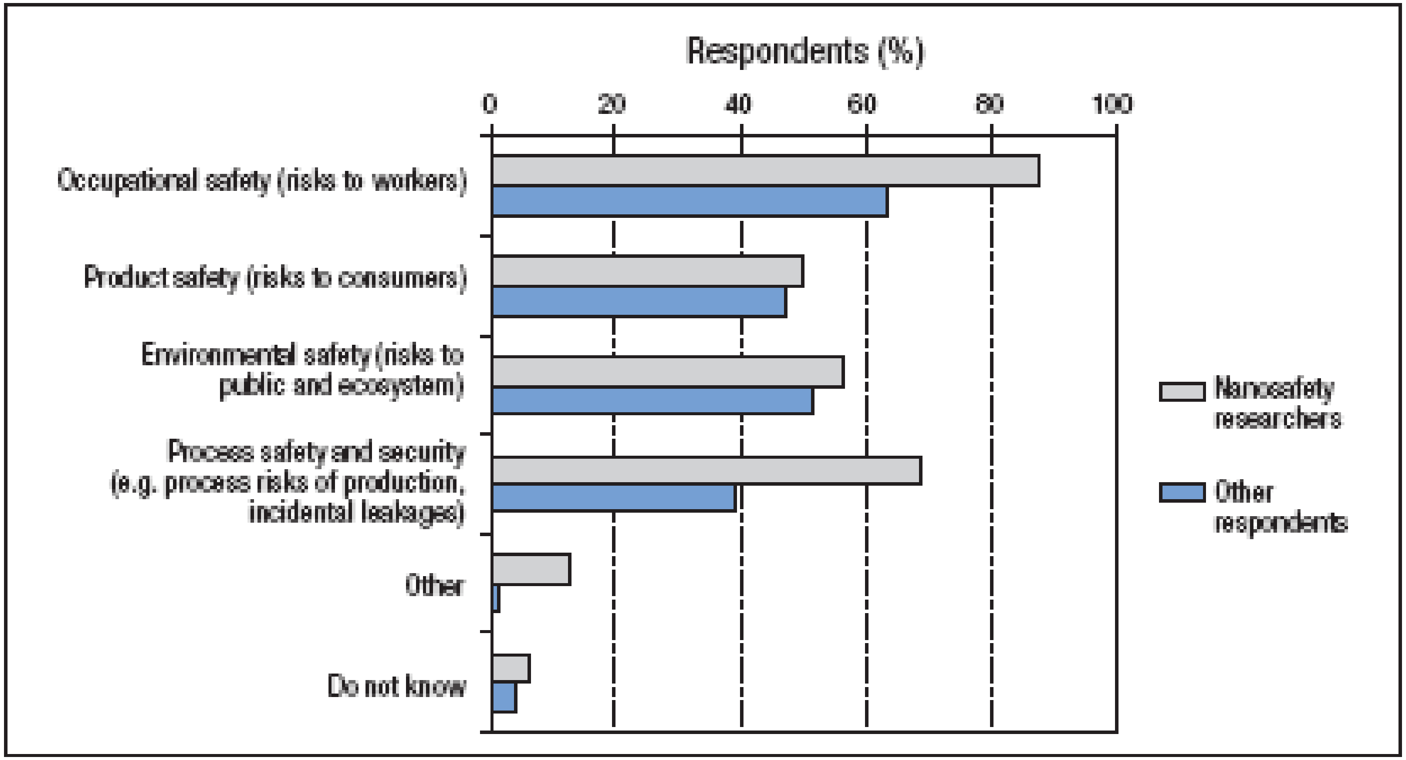
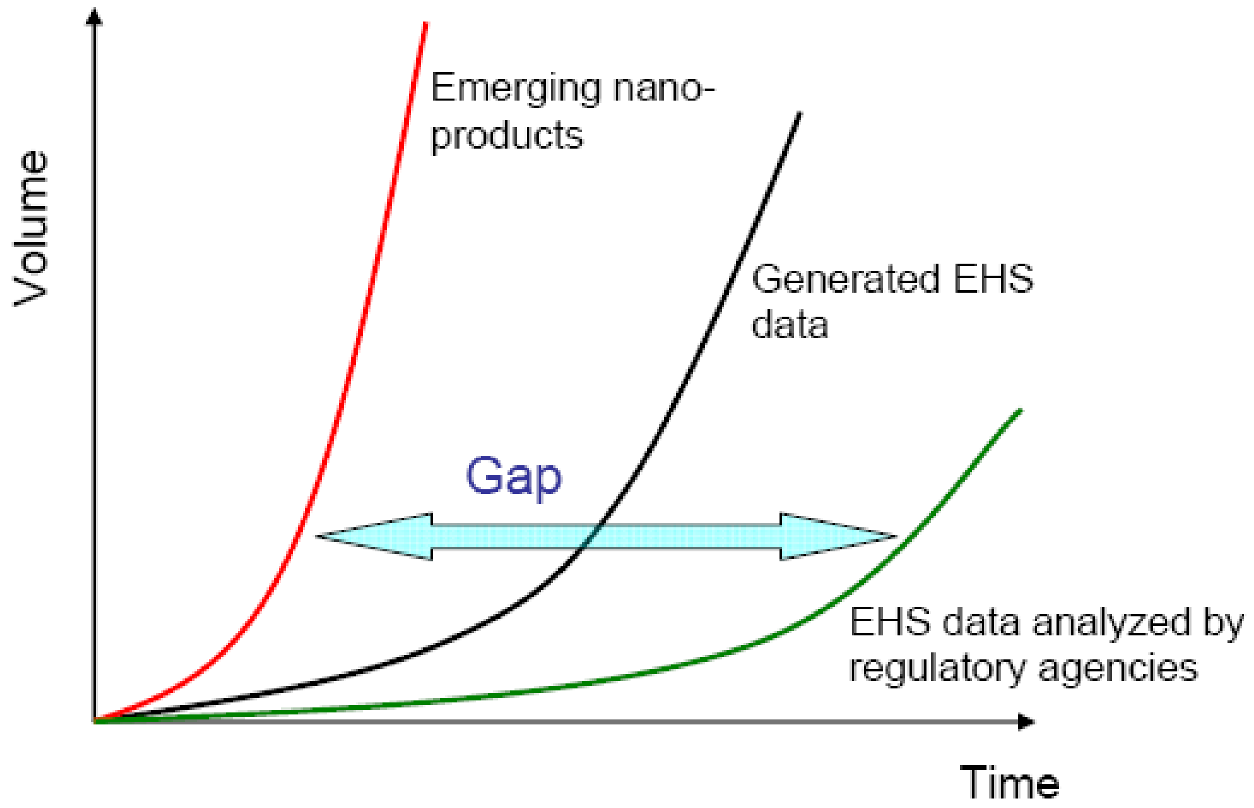


Figure 7. Future nanosafety related information needs

Raivio et al: Nanosafety in Finland – a summary report. Tekes, 2008

Challenges and conclusions: The safety knowledge gap



Schematic representation of emergence of nanotechnology products in comparison to generated EHS data (based on breakout group meeting, Canadian Workshop, Edmonton 2008).

Conclusions

- At present exposure most likely modest but real data on exposure or of exposed scanty; exposure levels and number of exposed workers on increase
- No complete data set available on health and safety on any given ENP – urgent need for generation of tiered testing approaches, data generation, development of simulating tools
- Some ENP cause deleterious effects, but are innocent
- Need to decouple ENP and nanotechnologies – need to identify hazardous ENP from safe ones to prioritize preventive actions

Acknowledgements

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- The views and opinions expressed in this presentation do not necessarily reflect those of the European Commission

4th International Conference on
Nanotechnology – Occupational and Environmental Health

- **Aims**

  The Conference will discuss global health and safety issues surrounding engineered nanoparticles and nanotechnologies, especially in connection with occupational and environmental health. The conference will also provide insights into the latest research results and actions to assure the safety and thereby the future success of nanotechnologies.

- **Background**

  Previous meetings in Taipei 2007, Minneapolis 2005, Buxton 2004

- **Preliminary themes of the Conference**
  - Characteristics of engineered nanoparticles
  - Exposure assessment to engineered nanoparticles
  - Toxicity and health effects of engineered nanoparticles
  - Effects of engineered nanoparticles on the environment
  - Control technologies and instrumentation: synthesis and characterization of exposure assessment
  - Risk assessment of engineered nanoparticles
  - Management and prevention of risks of engineered nanoparticles: reduction of exposure to engineered nanoparticles
  - Regulatory framework

- **Who should attend?**
  - Scientist and experts interested in the safety and health effects of nanoparticles, their characterization and exposure assessment; occupational and environmental health and safety experts; representatives of the nanotechnology industry; employers and employee organizations; policy-makers at national, regional and international levels; organizations funding nanotechnology research; and all key stakeholders in this area.

- **National Organizing Committee**
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  - VTT Technical Research Centre of Finland; and University of Kuopio: Jorma Jokiniemi
  - TEKES: Mikko Moisio, Markku Lämsä

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