

NanoToxicology Issues – concerns going to the market

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Overview

- What are nanoparticles
- Health, safety, and environmental uncertainties of nanotechnology
- Public perception
- Communications challenges
- Regulatory concerns

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Nanoparticles

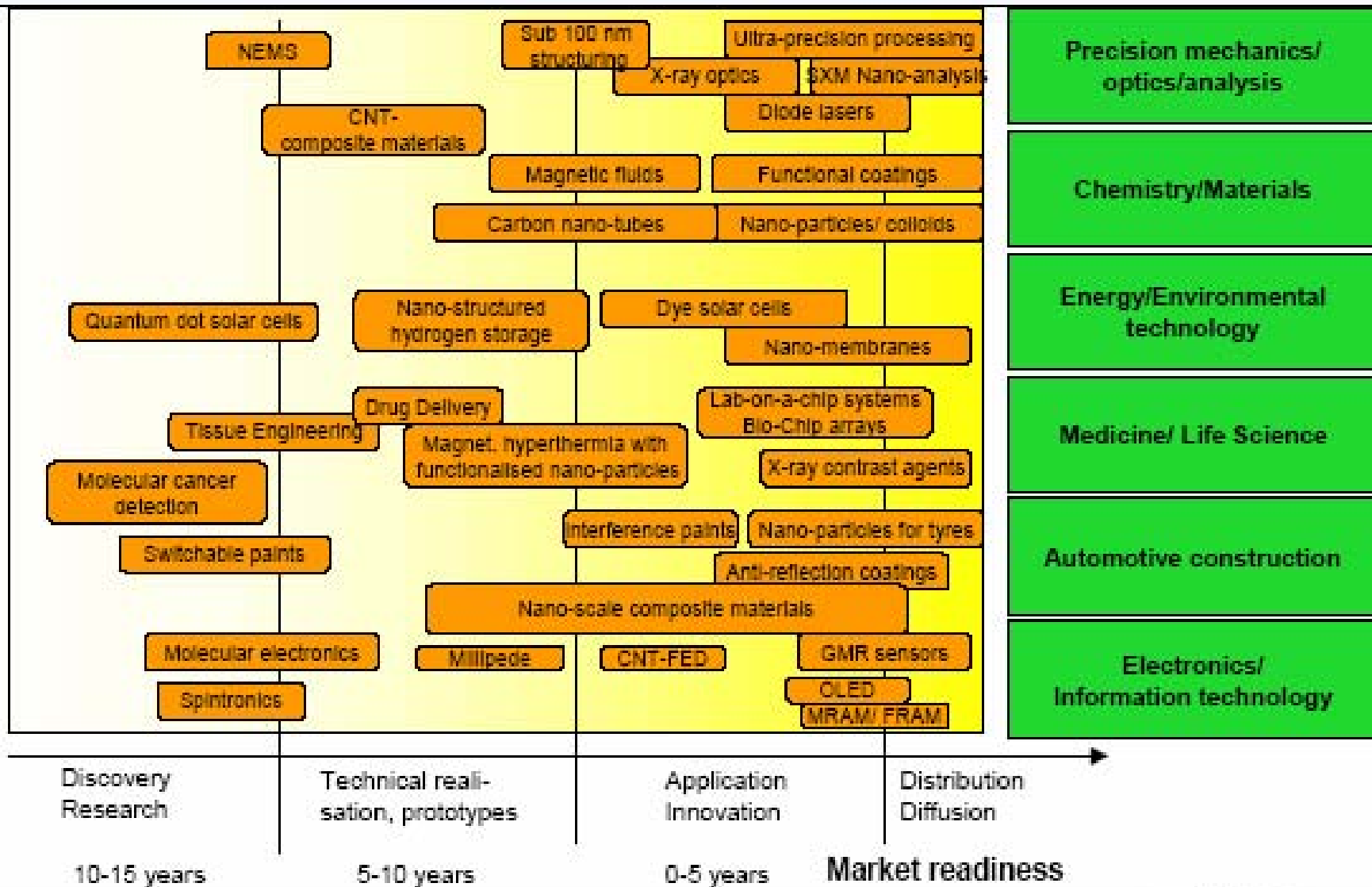
- **National Nanotechnology Initiative** definition:
Nanoparticle is an **engineered** or **designed** particle with at least one dimension < 100 nm.
 - Should have unique properties.

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Development status and application areas

The journey into the nano-world: II - Applications, products, markets



Health concerns of free particles

- We live in a cloud of small particles – generated from road dust to cooking food. Exposure to ambient particles has been associated with:
 - Respiratory disease
 - Cardiovascular disease
 - Immunosuppression and allergic responses
- Are the responses to ambient particles applicable to all free nanoparticles?

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Health concerns

- Nanoparticles have unusual effects or properties.
 - Smaller size and the surface chemistry have an impact on biological response for **some** nanomaterials.
 - Smaller size means greater chance for movement within the body to other locations.
 - If airborne is bad, is dermal safer?

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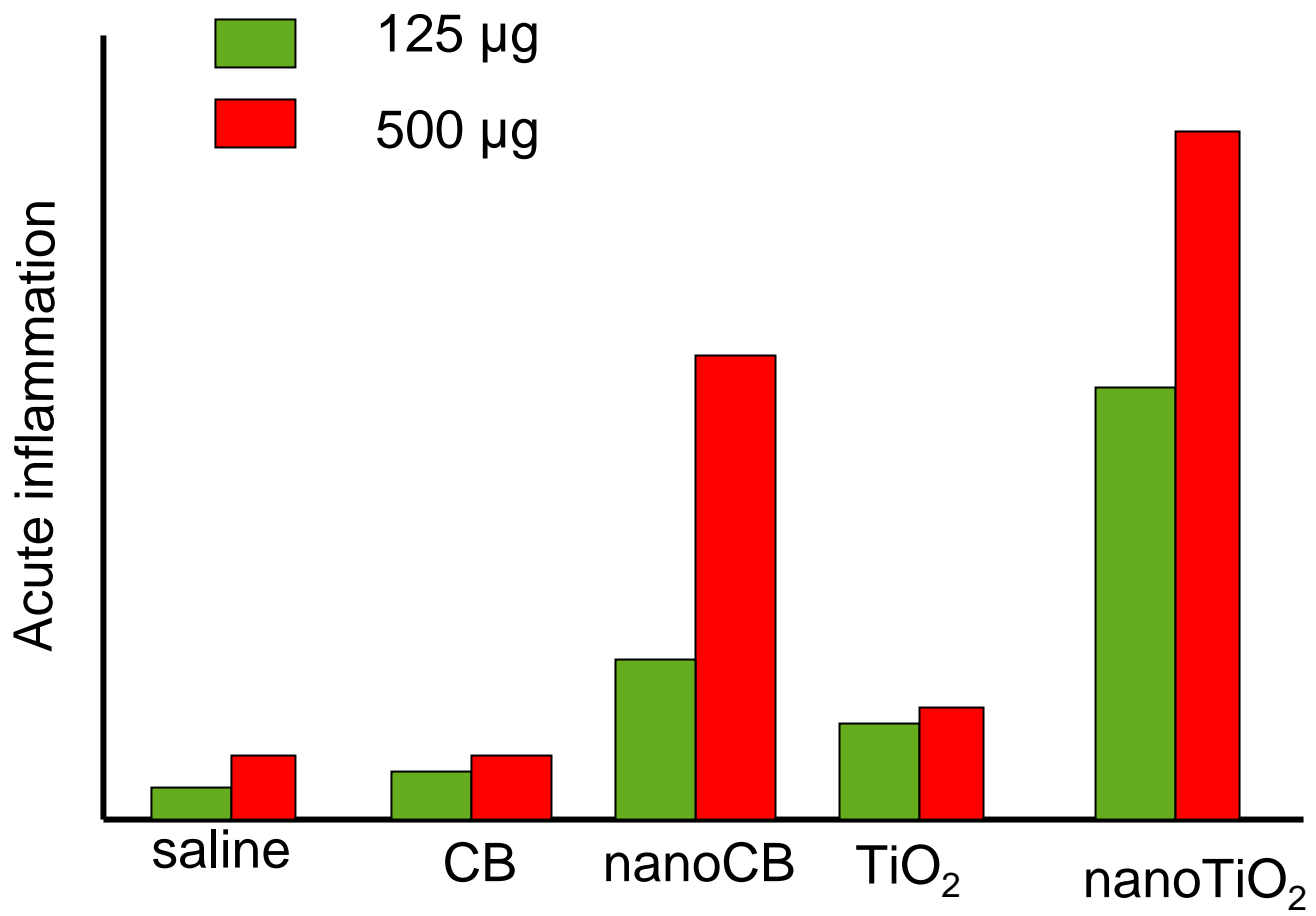
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Size matters

- Greater inflammatory response and greater cell damage for carbon black or TiO_2 if “nanosized”
 - 14.3 nm v 260 nm, or 29 nm v 250 nm (Renwick *et al.*, 2004).
- Bulk material considered to be “non-toxic”.

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From Renwick *et al.*, 2004.

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But not always

- Chen *et al.* (2004) observed less a fibrogenic response in rats treated with nano-SiO₂ than macro-SiO₂.
- Wang *et al.* (2006) observed only minor differences between responses of animals treated with nano-Zn compared with macro-Zn.
- Stoeger *et al.* (2006) suggest a threshold surface area dose of 20 cm² for pulmonary inflammatory response.

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Deposition and translocation

- NP can migrate from site of application. Traditional barriers no longer adequate.
 - Elemental Ag (17.1 nm) found in liver, kidneys, heart, posterior nasal cavity, **brain** (olfactory and other areas), and blood of rats 24 hours after inhalation (Takenaka *et al.*, 2001).
 - Solid lipid nanoparticles (200 nm) found in liver, kidneys, spleen, intestine, urine, and **testes** of rats 4 hrs after inhalation (Videira *et al.*, 2002).

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Deposition and translocation

- Dermal absorption of NPs not clear – key may be motion.
 - 500 and 1000 nm polystyrene beads penetrate “flexed” human skin, but not into “unflexed” skin (Tinkle *et al.*, 2003).
 - 20 nm TiO₂ particles from an oil-in-water emulsion did not penetrate the thick cell layer of cadaver skin (Pflucker *et al.*, 2001).

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Deposition and translocation

- Shape (area?) and surface chemistry also play a role in dermal penetration (Ryman-Rasmussen *et al.*, 2006).
 - Spherical quantum dots with neutral or carboxylate-coating remained in the epidermis, while amine-coated spheres penetrated to dermis.
 - Elliptical quantum dots with neutral or amine-coating remained in the epidermis, while carboxylate-coated spheres did **not** even penetrate the stratum corneum.

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Evaluating the hazards

- Several groups (OECD Nanotechnology Working Group, ACC Nanotechnology Panel, ILSI Nanotechnology Working Party, as well as national agencies) are developing testing schemes which consider the physical/chemical characteristics of nanomaterials:
 - Insolubility and dissolution rate
 - Size (and surface area) and surface chemistry
 - Agglomeration potential
 - Airborne versus liquid dispersed
 - Particles bound in a matrix versus free

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Dealing with the risks

- Good risk management procedures can be used to reduce the possibility of exposure.
 - Adequate environmental controls
 - Use of closed systems
 - Use of liquid-dispersed materials
 - Use of Personal Protective Equipment
 - Treat waste as hazardous; reduce the risk of releases to the environment by incorporating into a matrix

- Many companies using practices that are appropriate to the perceived risks until better information is available.

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Public perception

- Varies from:
 - Eddie Bauer pants with “nanoparticles” --- a good thing.

- To:
 - GM foods --- not a good thing.

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Communications challenges

- Understanding the public perception prior to marketing:
 - Eddie Bauer pants with nanoparticles
 - iPod 'nano'

- Educating the public after marketing:
 - Cosmetics
 - Unlike GM foods

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Regulatory uncertainties

■ General

- No regulatory definition of nanoparticle
- Are current regulations adequate to protect health and environment?
- What triggers regulatory review? CAS registry number? Size?

■ US

- EPA will initiate program to gather data on current products to help develop evaluation of new products.
- FDA will review its evaluation procedures for nanomaterials currently in use.
- CPSC has generic guidance document.

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Summary

- Nanotechnology presents a business opportunity for many companies.
- The uncertainties around safety present challenges to businesses and regulators, so reducing risks/exposure are important.
- A number of groups are working with regulators to reduce the uncertainties.
- Avoiding the mistakes of GM foods is foremost on the minds of many within government and industry.

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