OVERVIEW OF NANOTECHNOLOGY AND ITS RELATIONSHIP WITH SAFETY

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Occupational Safety and Health Administration

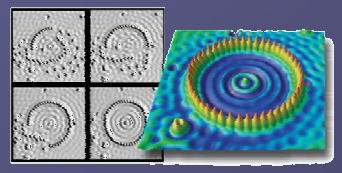
Disclaimer

The views expressed in this presentation do not necessarily reflect those of the Occupational Safety and Health Administration

Outline

- What is nanotechnology? Nanoscale materials? Examples; uses
- Health concerns
- Occupational exposure controls: NIOSH/U.K. HSE information
- Other US government activities
- Other UK reports

Nanotechnology
Definitions



Nanotechnology:

The manipulation of matter at nanometer length-scales to produce new materials, structures and devices with unique properties

Nanomaterials:

Intentionally created materials consisting of or containing designed components with dimensions < 100nm

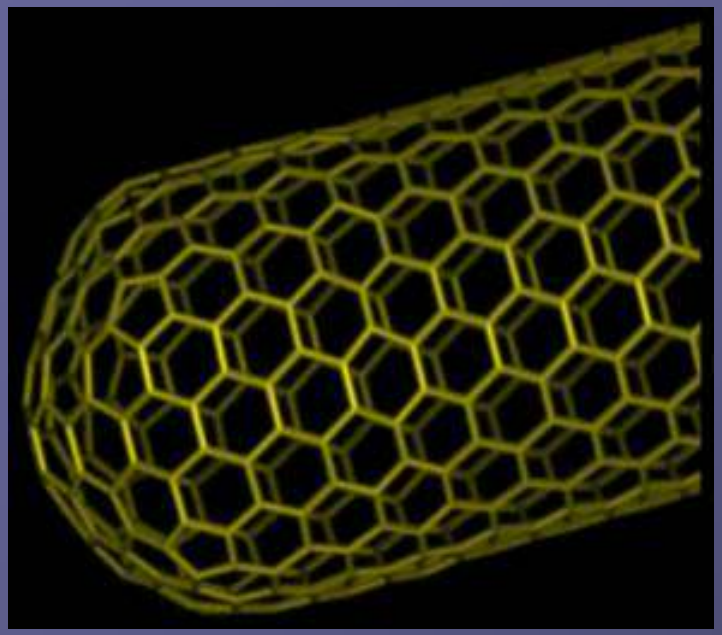
Nanoscale comparisons

- Nanoscale: 100 nm down to size of atoms (approximately 0.2 nm)
- Single human hair: 80,000 nm
- Red blood cell: 7,000 nm
- Water molecule: 0.3 nm

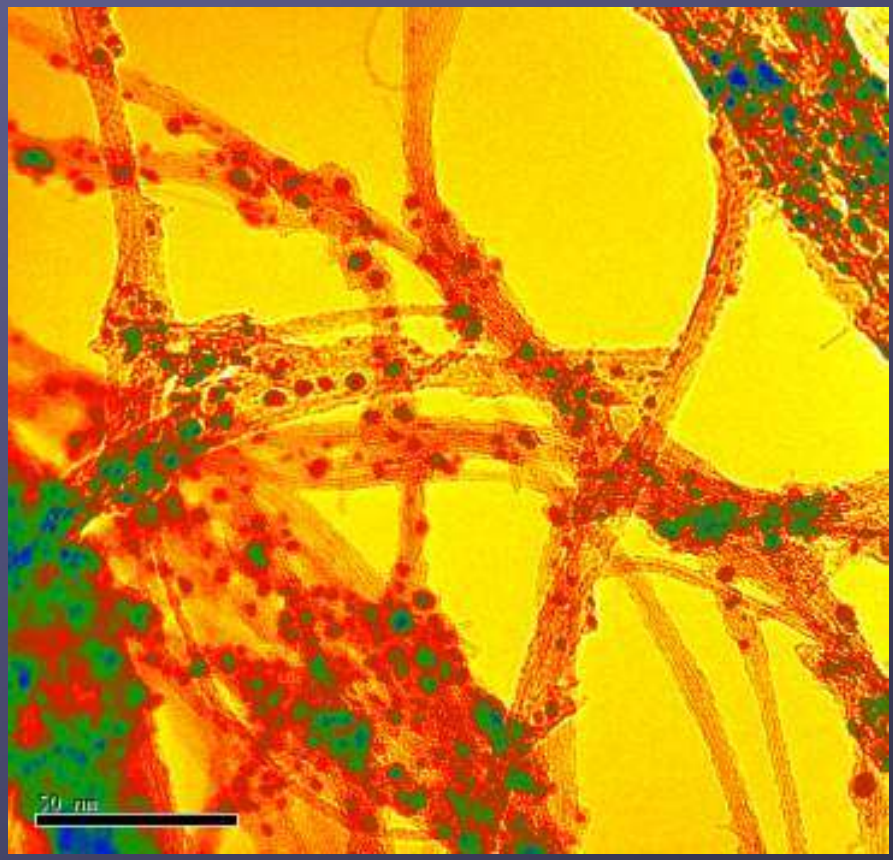
Examples of Nanomaterials

- Carbon nanotubes
- “Bucky balls” and other fullerenes
- Quantum dots
- TiO_2

Single Walled Carbon Nanotubes

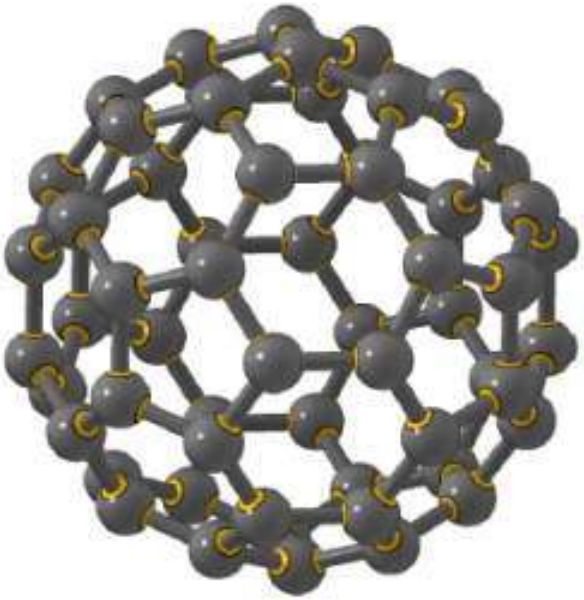


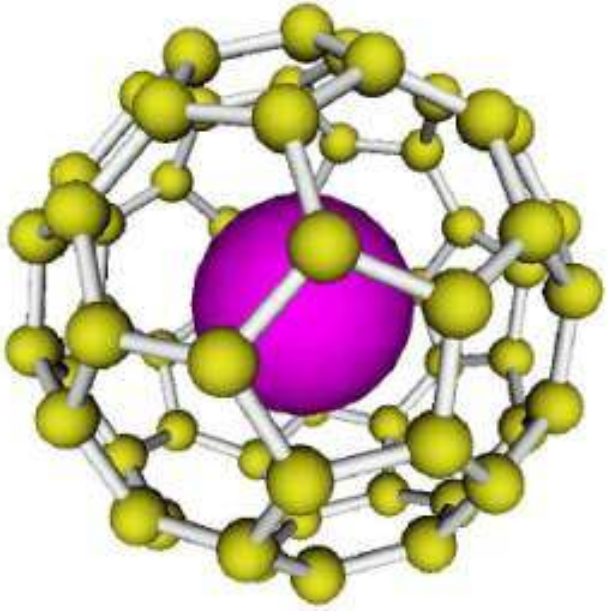
- 1.4 nm in diameter
- Micrometers in length
- Unique physical, chemical and electronic properties



Transmission Electron Microscopy

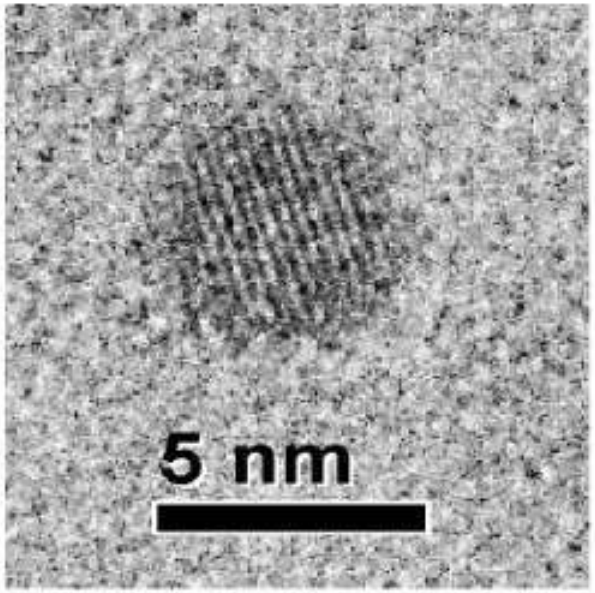
"Bucky Balls" and other Fullerenes



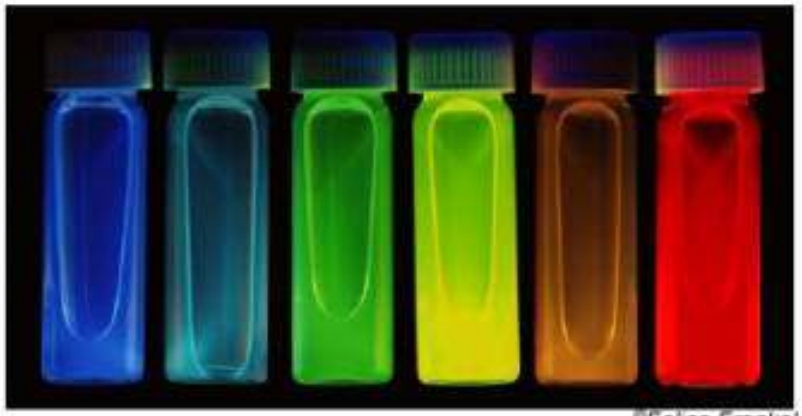


- 60 carbon molecule named in honor of R.Buckminster Fuller
- Can encase other molecules.

Quantum Dots



Images from Andrew Maynard presentation.



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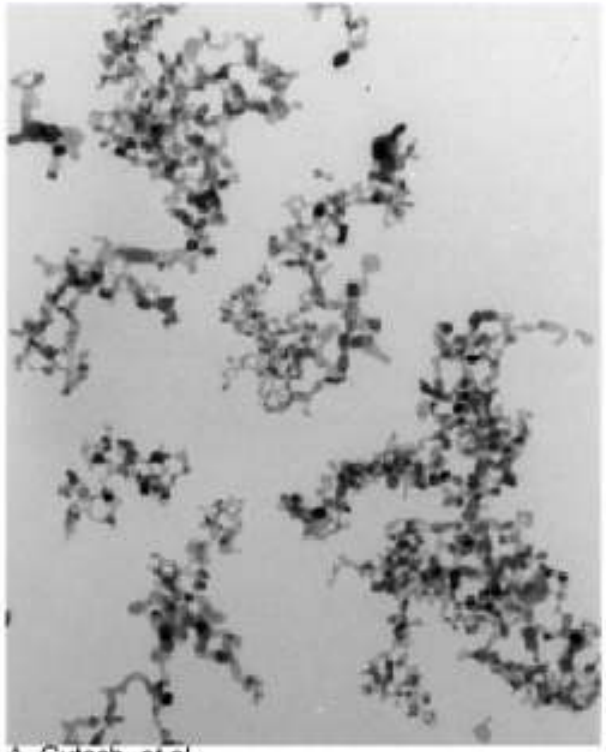
Quantum Dots

- Semiconductor structures in the low nanometer range.
- Fluorescent wavelength dependant on size.
- Can be attached to bio-molecules.

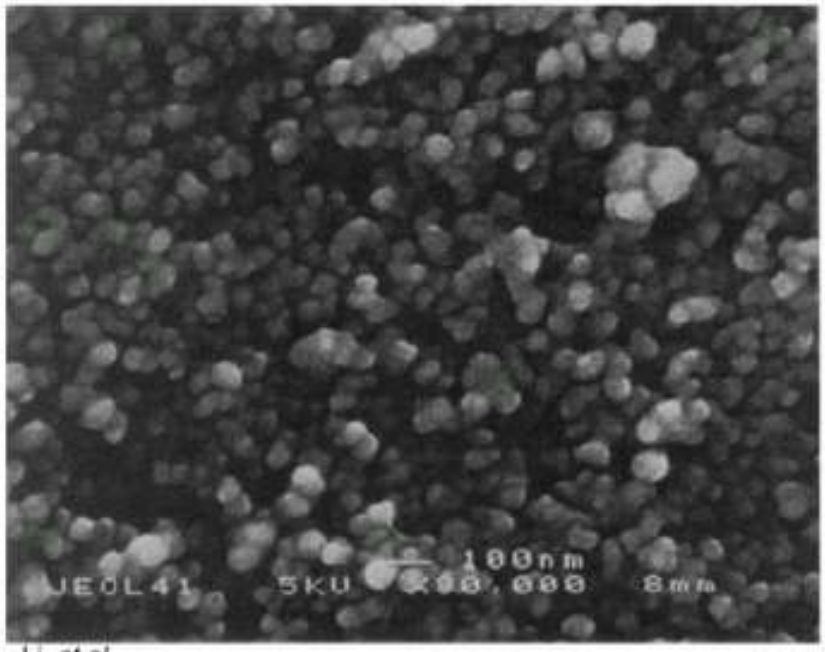
Uses of Nanotechnology

- Current: electronic, magnetic and optoelectronic, biomedical, pharmaceutical, cosmetic, energy, catalytic and materials applications.
- Next 2-5 years: Advanced drug delivery systems; medical diagnostic tools- cancer tagging mechanisms; cooling chips or wafers to replace compressors; sensors for airborne chemicals or other toxins; photovoltaics (solar cells), fuel cells
- Future: composites; lubricants

Nanoparticles



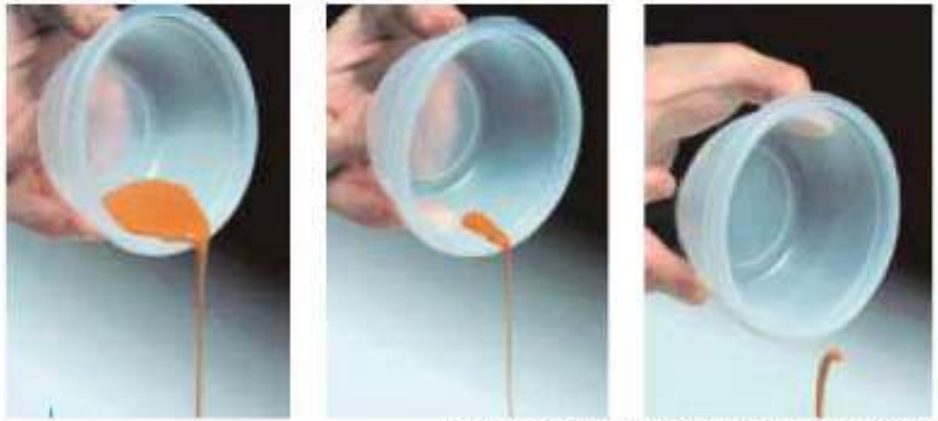
A. Gutsch, *et al*,



Li, *et al*,

- Left: ZrO_2 nanoparticles with a surface area of 74 m^2/gm.
- Right: SEM Micrograph of TiO_2, as used in sunscreen.

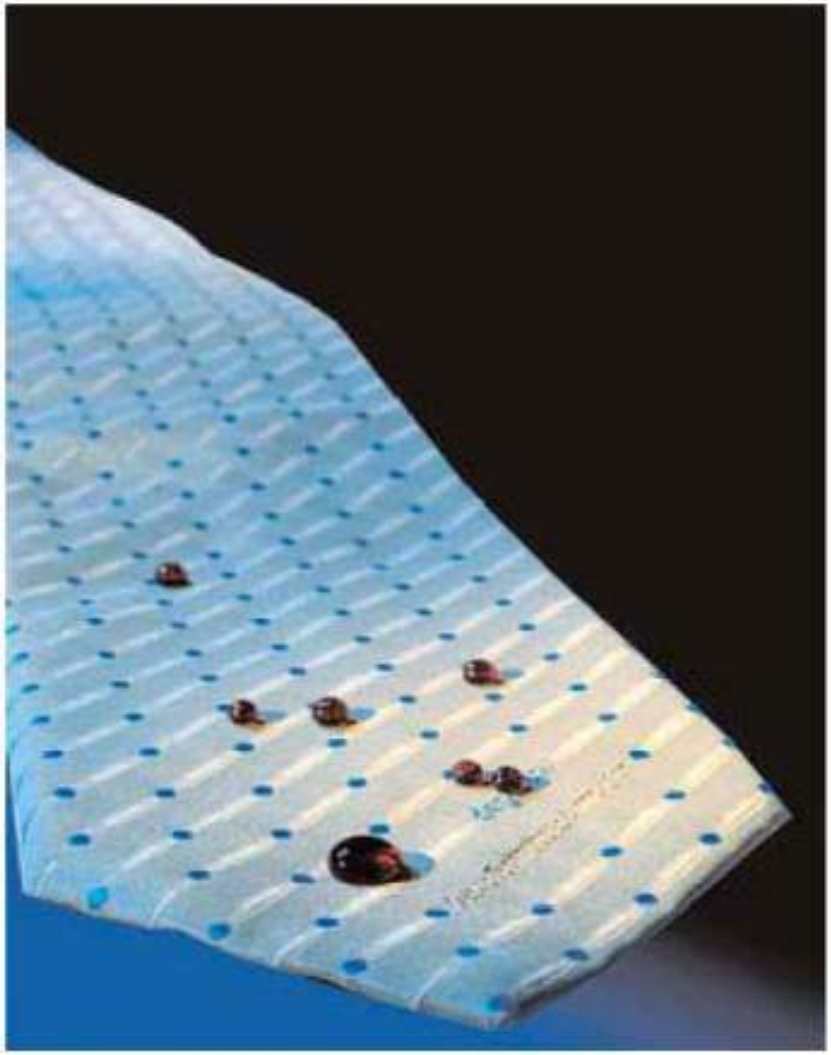
Other Materials and Applications



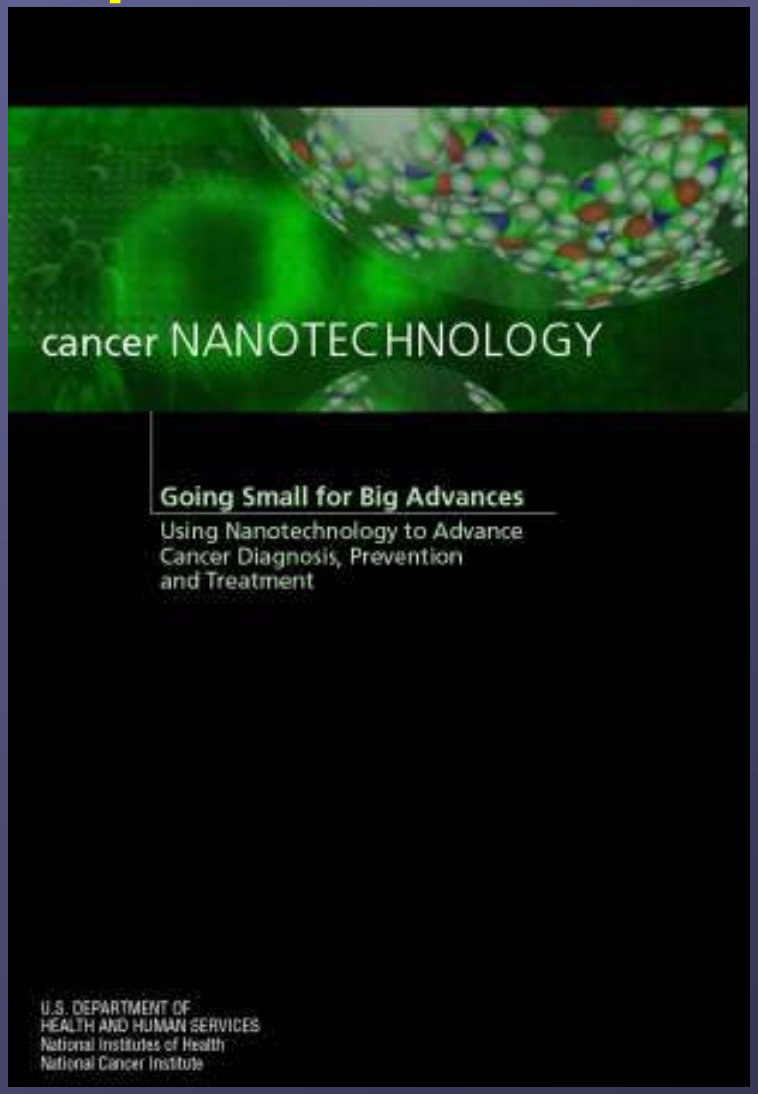
Degussa Science Newsletter, Feb, 2003

"Super Hydrophobic" water and stain resistant surfaces.

Nano sized modified amorphous silica bound to surfaces.



Cancer diagnosis, treatment, prevention



Prevention and control of cancer

- Developing nanoscale devices that can deliver cancer prevention agents
- Designing multicomponent anticancer vaccines using nanoscale delivery devices

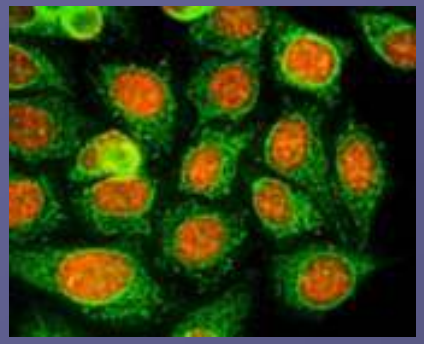
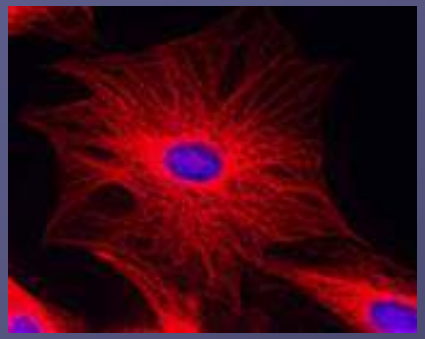
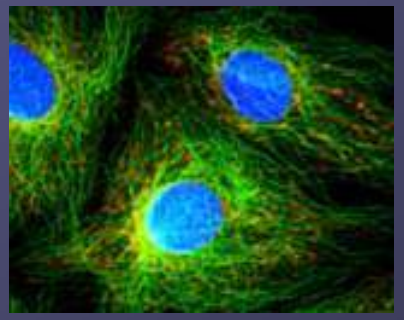
Early detection and proteomics

- Creating implantable, biofouling-indifferent molecular sensors that can detect cancer-associated biomarkers that can be collected for *ex vivo* analysis or analyzed *in situ*, with the results being transmitted via wireless technology to the physician
- Developing “smart” collection platforms for simultaneous mass spectroscopic analysis of multiple cancer-associated markers

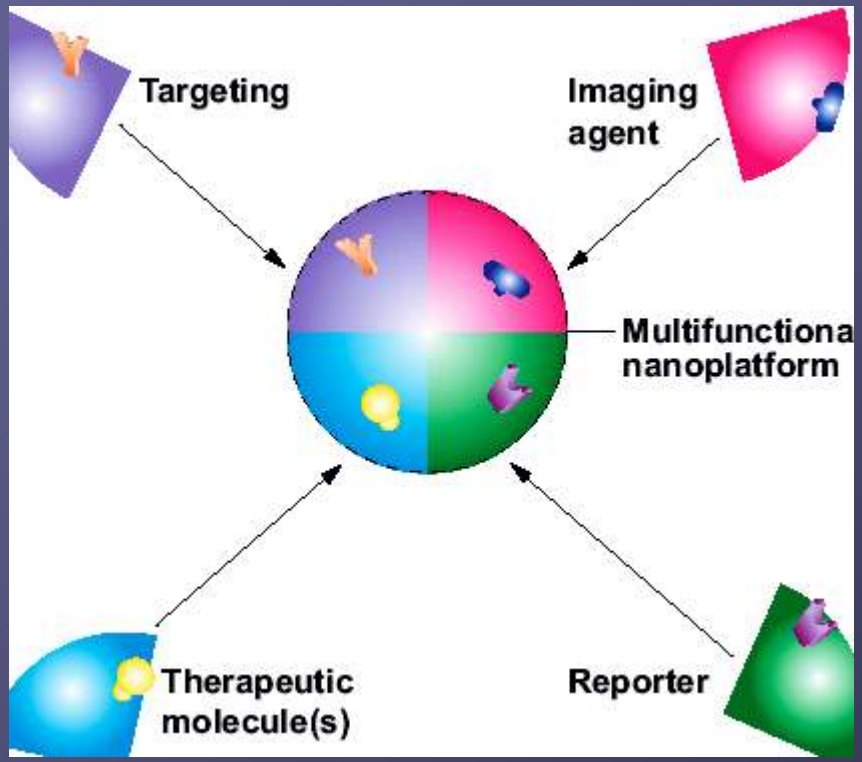
Multifunctional therapeutics

- Developing nanoscale devices that integrate diagnostic and therapeutic functions
- Creating “smart” therapeutic devices that can control the spatial and temporal release of therapeutic agents while monitoring the effectiveness of these agents

Quantum dots

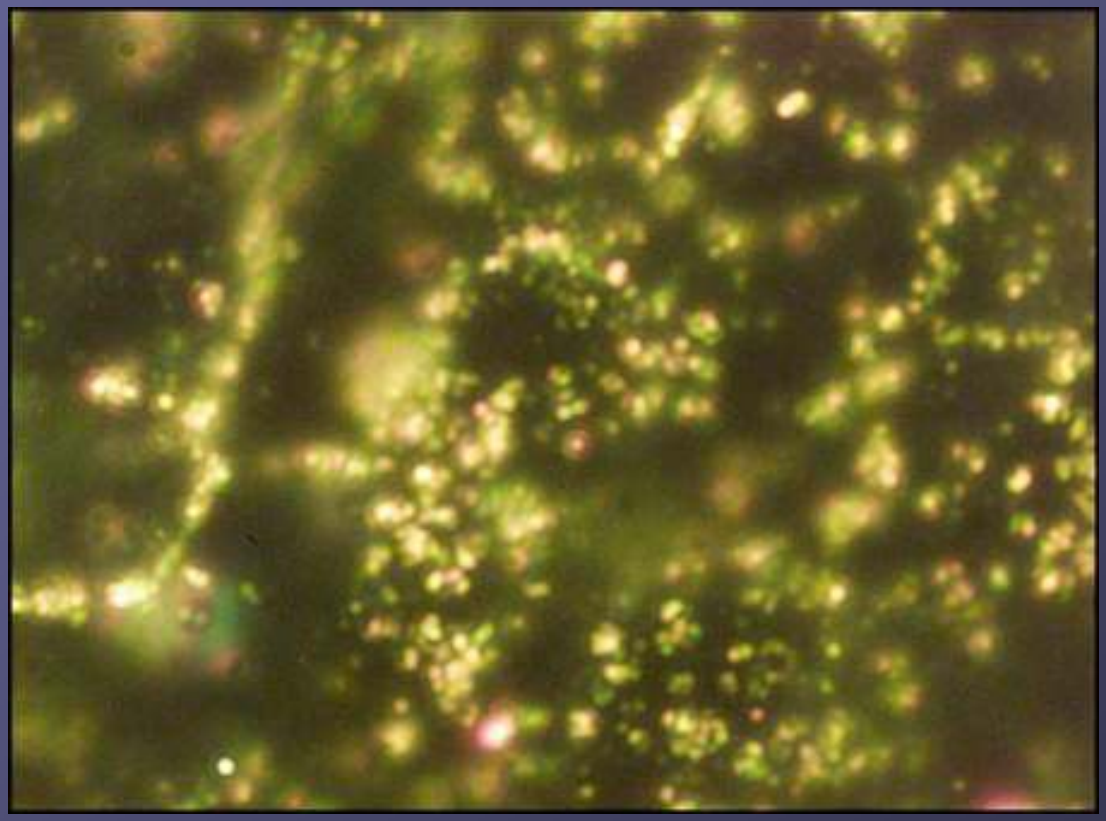




- Because of multitude of colors, can be combined to detect multiple substances at once
- E.g., researchers simultaneously measured levels of breast cancer marker Her-2, actin, microfibril proteins, and nuclear antigens.

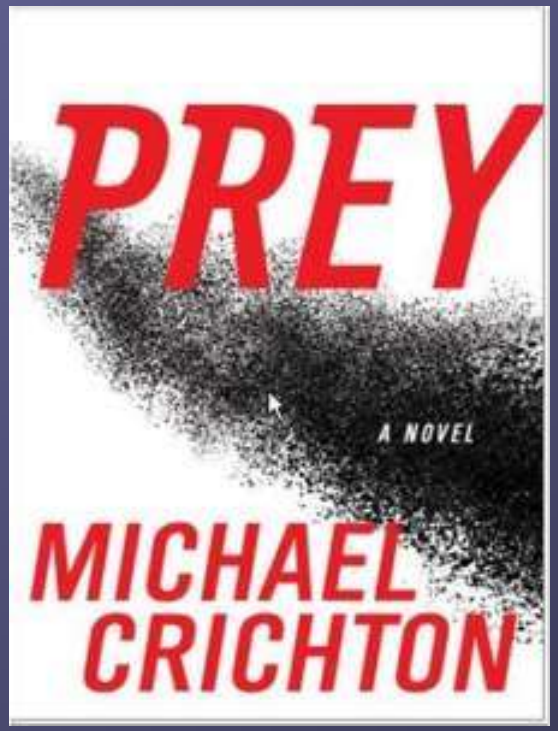

Targeting
Imaging agent
Multifunctiona nanoplatform
Therapeutic molecule(s)
Reporter

All that glitters…

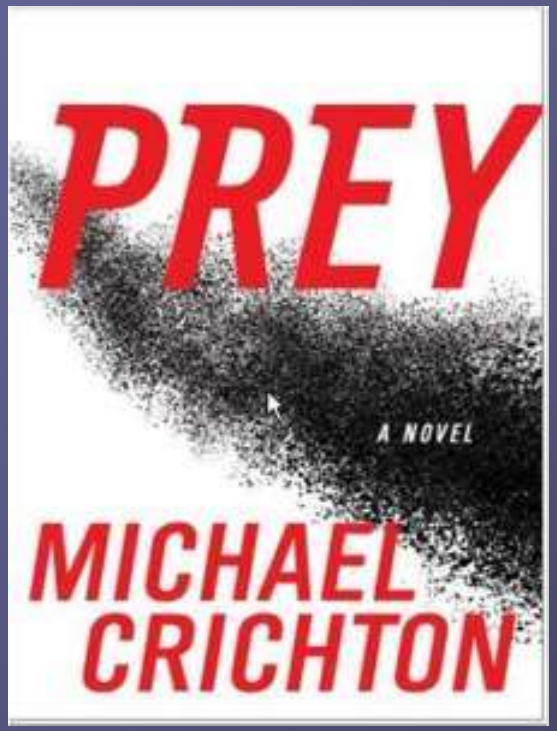
(Washington Post, 5/24/05)



Nanomachines, programmed with predator/prey software…a swarm loose and multiplying, and appear to be carnivorous.

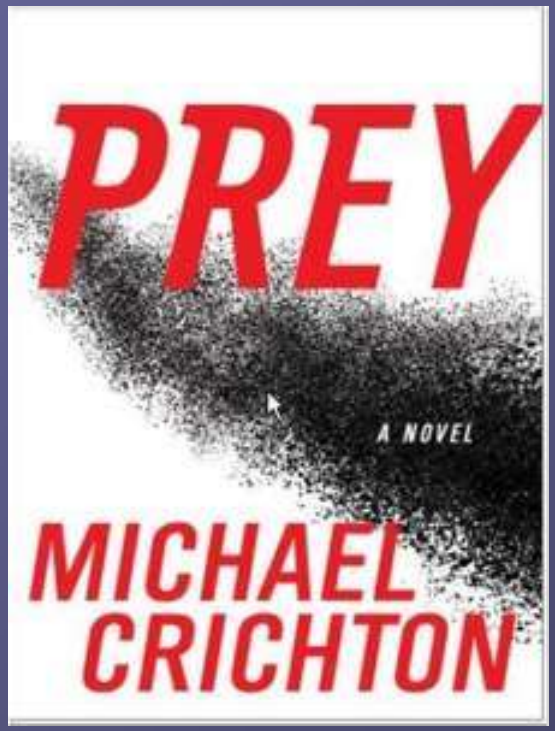


Excerpt:



- “Basically, I told them we had a **runaway swarm** we couldn't control. And the swarm exhibited self-organizing behavior.”

Excerpt:



- "... His lips were coated with swirling black residue. He started to have trouble breathing. Rosie was still screaming as the **second swarm** descended on David, and the black spread across his face, onto his eyes, into his hair. His movements became increasingly ..."

Health concerns

- Very properties that make nanoparticles useful might also have negative health impacts
- Nanoparticles may interact with the human body in different ways than conventional materials, due to their extremely small size

Types of Nanoparticles

- Engineered/intentional
  - e.g., metals, semi-conductors, fullerenes, quantum dots/rods, nanotubes; nanoclays, micronized
- Incidental/unintentional
  - e.g., internal combustion engines, power plants, incinerators, metal fumes (welding, smelting), cooking (frying, grilling)
- Natural sources
  - e.g., forest fires, volcanoes, viruses

➢ *What can we learn from studies of existing nanoparticles about the potential health risk of new nanomaterials?*

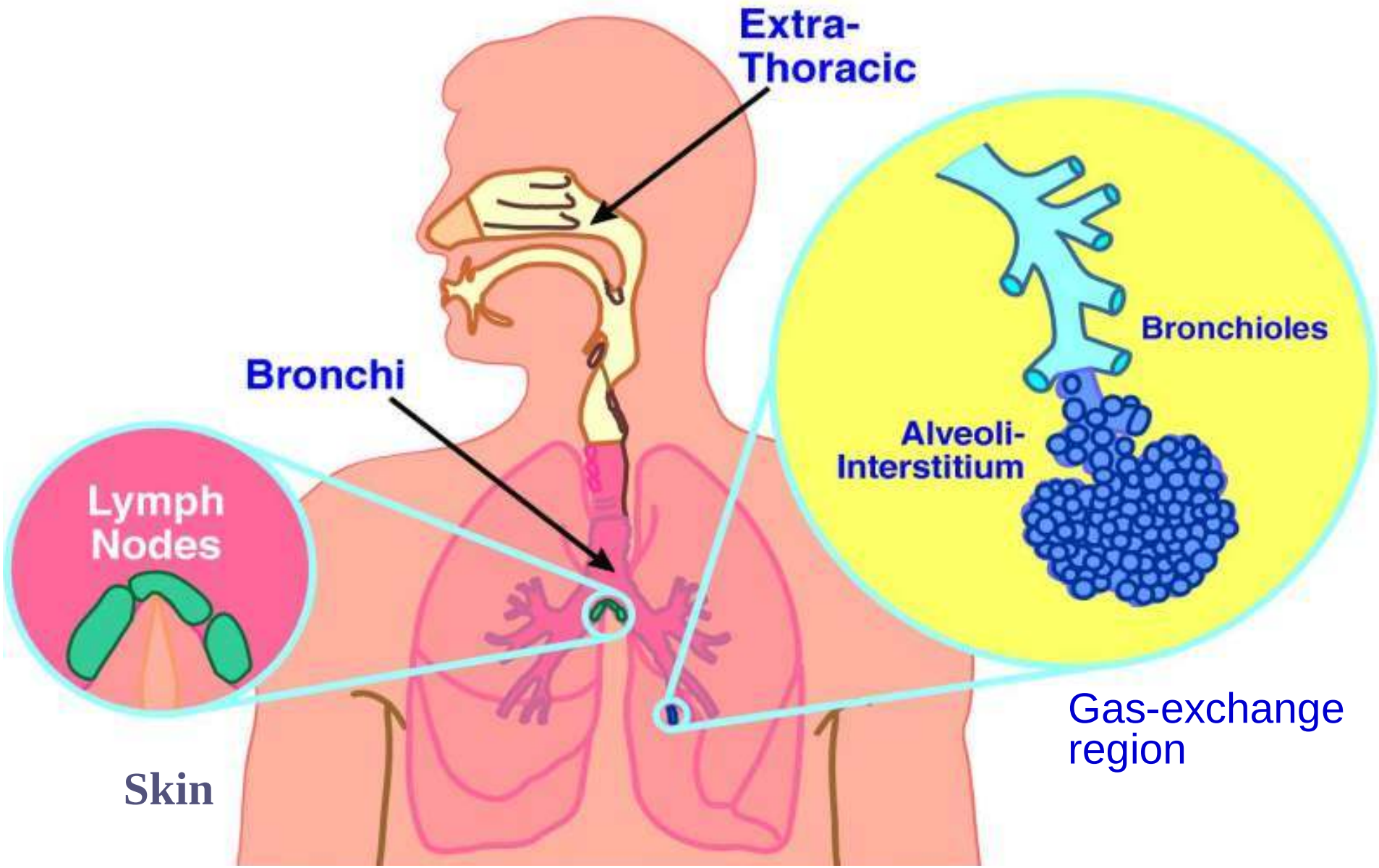
Respirable Particles: Capable of depositing in the alveolar (gas-exchange) region of the lungs

Nano (ultrafine)	<0.1 µm
Fine	0.1-2.5 µm
Coarse	2.5-10 µm

Dose Metric Matters: For equal particle mass…

Metric	Fine (2 µm)	**UF (20 nm)**
Mass	1	1
Surface area	1	100
Number	1	1,000,000

ANATOMICAL COMPARTMENTS OF THE RESPIRATORY TRACT



Particle Deposition in Human Respiratory Tract

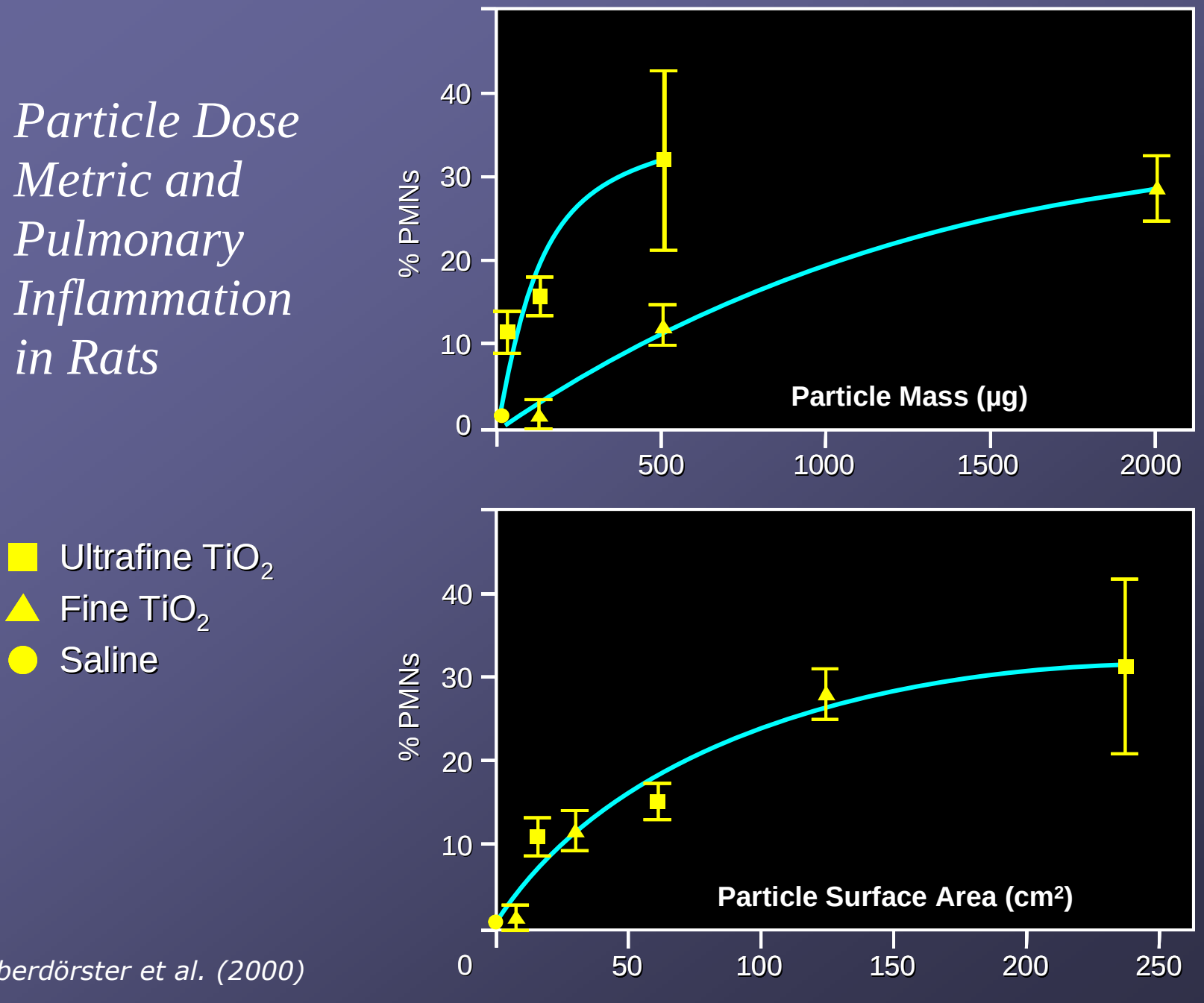
- Total deposition fraction increases to >90% as particle size decreases in nanoparticle range.
- Alveolar deposition fraction is several times higher for ultrafine than fine particles
  - ~20-50% for 5-100 nm *vs.* 2-15% for 0.2-10 μm (ICRP 1994)
- Total nanoparticle deposition is higher with:
  - ***Exercise:*** Particle number increases by 4.5 times (due to increases in both deposition and minute ventilation) (Daigle et al. 2003).
  - ***Breathing pattern:*** longer respiratory time (Jaques & Kim 2000).
  - ***Lung disease***, e.g., asthma or COPD (Brown et al. 2002).

Clearance and Translocation of Inhaled Particles: Animal Studies

- Nanoparticles escape alveolar macrophage phagocytosis and clear more slowly *(Renwick et al. 2001, 2004)*
- Increased retention in lung interstitum *(Ferin et al. 1992)*
- May enter blood and translocate to other organs, e.g., heart, liver, spleen *(Stone and Godleski 1999; Nemmar et al. 2002; Oberdörster et al. 2002; Kreyling et al. 2002)*
- Path to brain for nanoparticles depositing in nasal region, via olfactory nerve *(Oberdörster et al. 2004)*

Other exposure routes in workers: ingestion; dermal *(Tinkle et al. 2003)*

Particle Dose Metric and Pulmonary Inflammation in Rats

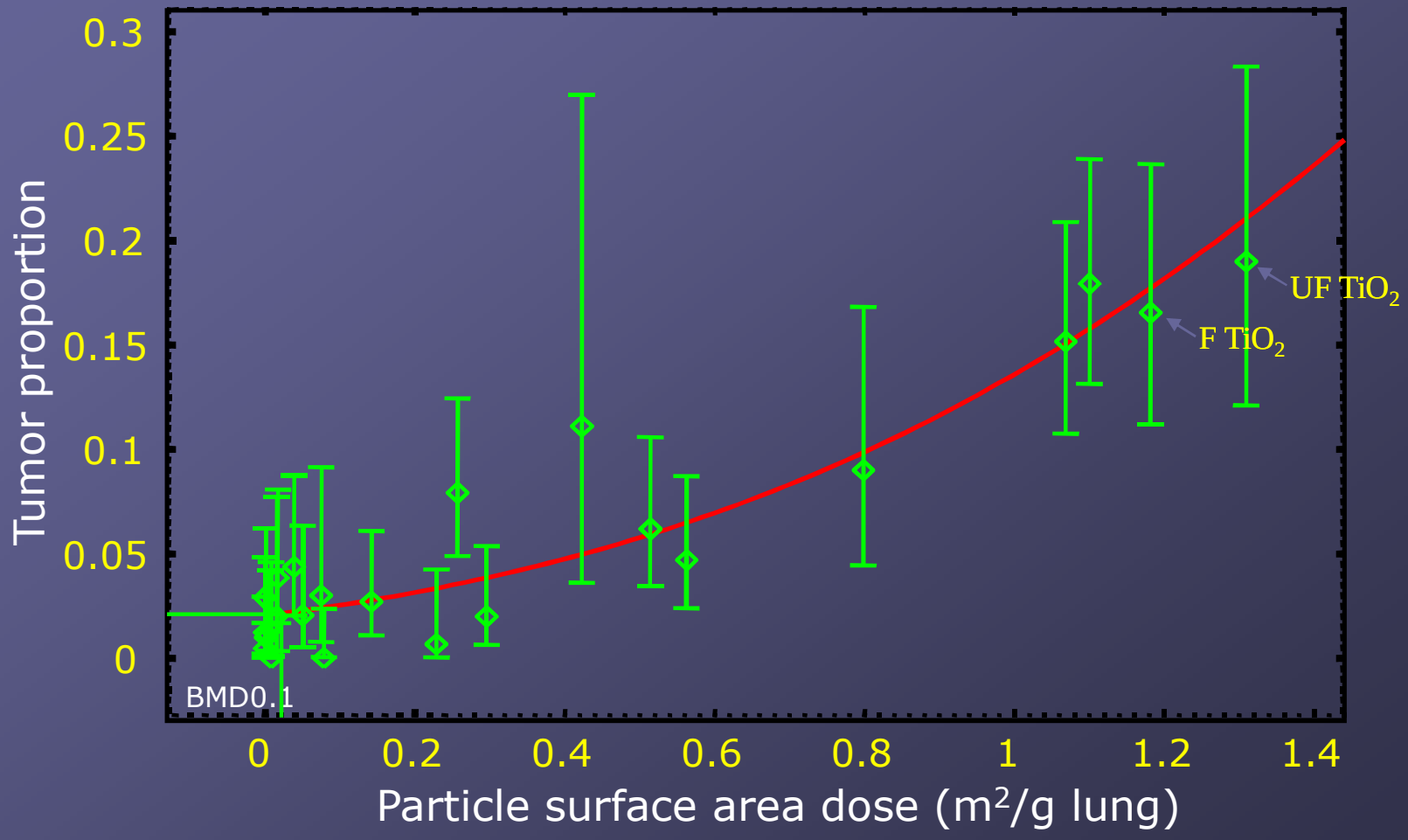


- Ultrafine TiO_2
- Fine TiO_2
- Saline

Oberdörster et al. (2000)

Chronic Inhalation Cancer Bioassays in Rats

diesel exhaust, carbon black, coal, titanium dioxide & toner



Animal Studies of Existing Nanoparticles

- *Compared to equal mass of larger particles of similar composition:*
  - Nanoparticles are more toxic *(oxidative stress; pulmonary inflammation and injury)* and more tumorigenic in rat lungs.
  - Particle surface area is better metric for predicting toxicity and carcinogenicity of inhaled particles.
- Size of particles influences deposition and ability to translocate beyond lungs.
- Surface reactivity is an important factor influencing particle toxicity.

Carbon Nanotubes:

"…totally insoluble and probably one of the most biologically nondegradable man-made materials." *(Lam et al. 2004)*

- Rats (instillation): *Warheit et al. (2004)*
  - Doses: ~0.02 and 0.1 mg (raw CNT, w/ Ni & Co)
  - Mortality (15%) w/in 24 hrs due to airway blockage
  - Multi-focal granulomas (not dose-dependent); transient inflammation
- Mice (instillation): *Lam et al. (2004)*
  - Doses: 0.1 and 0.5 mg (raw, purified, & iron-containing)
  - Ni-containing CNT: ~50% mortality w/in 7 days (0.5 mg)
  - All CNTs produced granulomas & inflammation (dose-dependent)
  - More toxic than quartz on mass basis

Human Studies with Nanoparticle Component

(Precise role of the nanoparticle component is unknown)

- Elevated lung cancer observed in some studies, but no exposure-response
  - Titanium dioxide, carbon black, diesel exhaust, welding fume
- Fibrosis
  - Beryllium, manganese, welding fume
- Respiratory symptoms and decreased lung function
  - Titanium dioxide, air pollution (PM2.5 and UF)
- Immunological response (sensitization)
  - Beryllium
- Neurological, psychomotor
  - Manganese

Bacteria and buckyball clumps
(Washington Post, 5/16/05)

- Hughes et al, June 1 Environ. Sci. Tech
- Until recently, it was thought that buckyballs not soluble in water
- Buckyballs clump and dissolve
- Bacteria exposed to buckyball clumps in water had reduced respiration and failed to reproduce

Buckyball clumps (continued)

- “Currently, regulations relating to workplace exposures to [buckyballs] and acceptable levels of environmental contamination are virtually identical to the rules for other, relatively nontoxic forms of pure carbon, such as graphite.”
- Researchers concluded that their results suggest a need for new nanomaterial safety standards

Control of Workplace Exposure

- Nanoparticles behave as a gas
- Enclosures, LEV, fume hoods, general ventilation need to be of a design suitable for gasses
- Effectiveness may be variable and is dependent on maintenance and worker behavior

Filtration

- HEPA for ventilation systems, N- P- R-100 for respirators
- Not tested with nanoscale particulate, but expected to be effective
- Question of effectiveness for smallest particles (<= 2 nm)

- Respirator faceseal leakage probably same as for gasses
- Dermal protective equipment not tested for penetrability of nanomaterials
- Transfer to skin from outer clothing surface – human factors critical given high mobility and surface area of nanoparticulate

Working with Engineered Nanomaterials
NIOSH **Information**

- **Nanotechnology topic page**

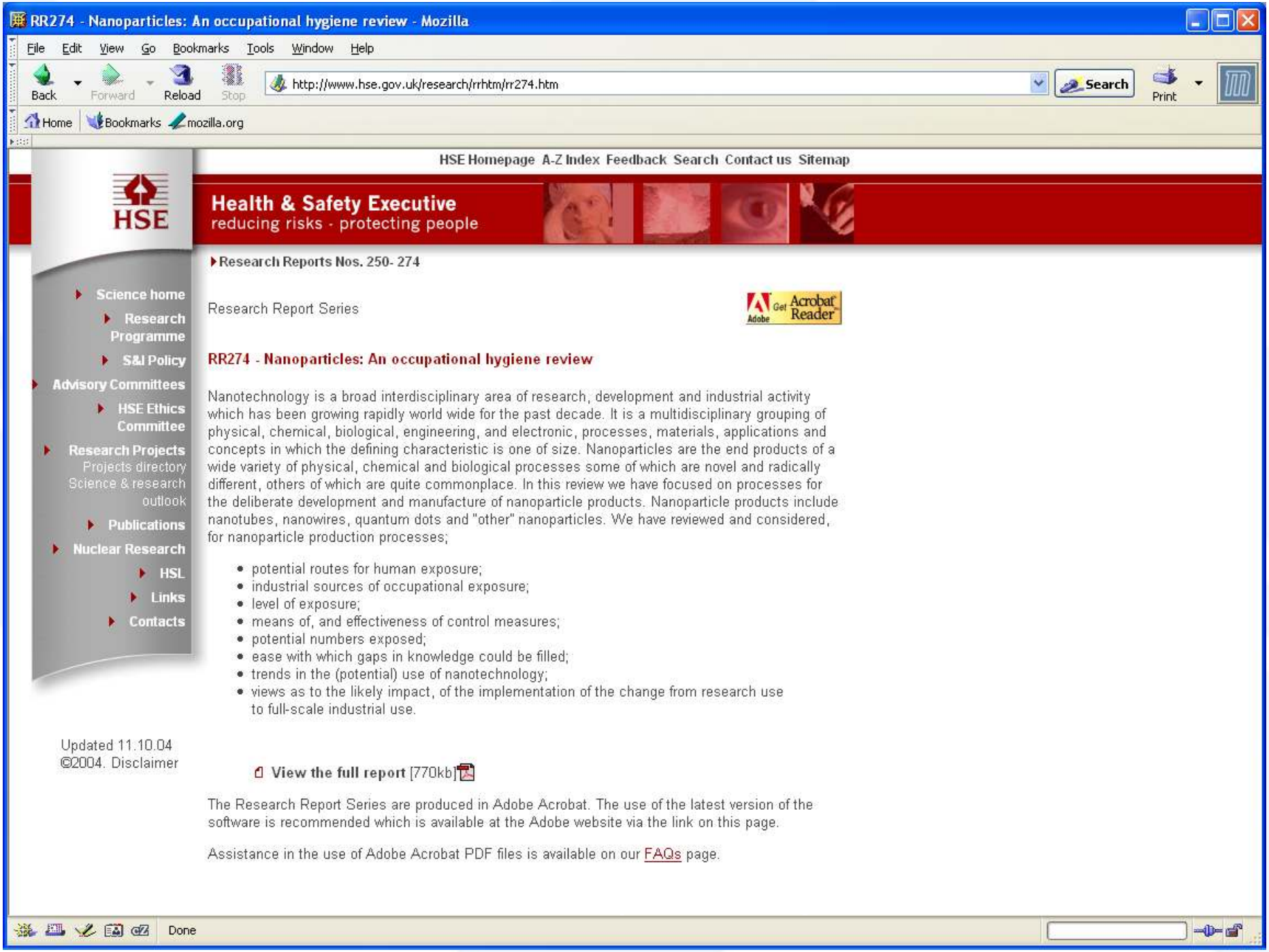
- Fact Sheet
  - Raise awareness on nanotechnology and occupational health

UK nanotechnology exposure control information

- Health and Safety Executive:

  Nanoparticles: An Occupational Hygiene Report

  http://www.hse.gov.uk/research/rrhtm/rr274.htm


RR274 - Nanoparticles: An occupational hygiene review - Mozilla
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RR274 - Nanoparticles: An occupational hygiene review
Nanotechnology is a broad interdisciplinary area of research, development and industrial activity which has been growing rapidly world wide for the past decade. It is a multidisciplinary grouping of physical, chemical, biological, engineering, and electronic, processes, materials, applications and concepts in which the defining characteristic is one of size. Nanoparticles are the end products of a wide variety of physical, chemical and biological processes some of which are novel and radically different, others of which are quite commonplace. In this review we have focused on processes for the deliberate development and manufacture of nanoparticle products. Nanoparticle products include nanotubes, nanowires, quantum dots and "other" nanoparticles. We have reviewed and considered, for nanoparticle production processes;
potential routes for human exposure;
industrial sources of occupational exposure;
level of exposure;
means of, and effectiveness of control measures;
potential numbers exposed;
ease with which gaps in knowledge could be filled;
trends in the (potential) use of nanotechnology;
views as to the likely impact, of the implementation of the change from research use to full-scale industrial use.
Updated 11.10.04
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Assistance in the use of Adobe Acrobat PDF files is available on our FAQs page.
Done

Other US Government Nanotechnology Information

- **National Nanotechnology Initiative (NNI)**
  - Interagency coordination of nanotechnology R&D
  - US R&D funding:
    - $1 billion for FY04
    - Estimated at >$3.7 billion for 2005 – 2008

www.nano.gov

Other UK nanotechnology information

- Royal Society and Royal Academy of Engineering:

  Report on nanotechnologies

  http://www.nanotec.org.uk/

Aims of the Royal Society Study

- “define what is meant by nanoscience and nanotechnology;
- summarise the current state of scientific knowledge about nanotechnology;
- identify the specific applications of the new technologies, in particular where nanotechnology is already in use;
- carry out a forward look to see how the technology might be used in future, where possible estimating the likely time scales in which the most far-reaching applications of the technology might become reality;
- identify what environmental, health and safety, ethical or societal implications or uncertainties may arise from the use of the technology, both current and future;
- identify areas where regulation needs to be considered.”

Recent UK government report

- February 2005
- Responds to the earlier report from the two British science academies
- Concludes that "unbound" nanoparticles (as opposed to those embedded in solid materials) should be kept out of people's bodies and the environment as much as possible until their risks are better understood; new safety regulations should be created for nanoparticles; and the government should consider requiring labeling of consumer products containing unbound nanoparticles -- including some cosmetics already on the market -- so consumers can decide whether to use them.
- http://www.ost.gov.uk/policy/issues/nanotech_final.pdf

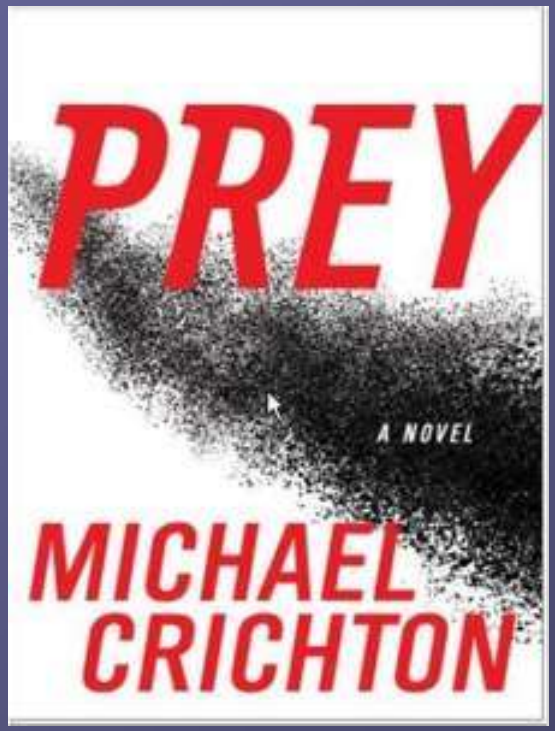
Precautionary Principle

"The precautionary principle demands the proactive introduction of protective measures in the face of possible risks, which science at present – in the absence of knowledge – can neither confirm nor reject."

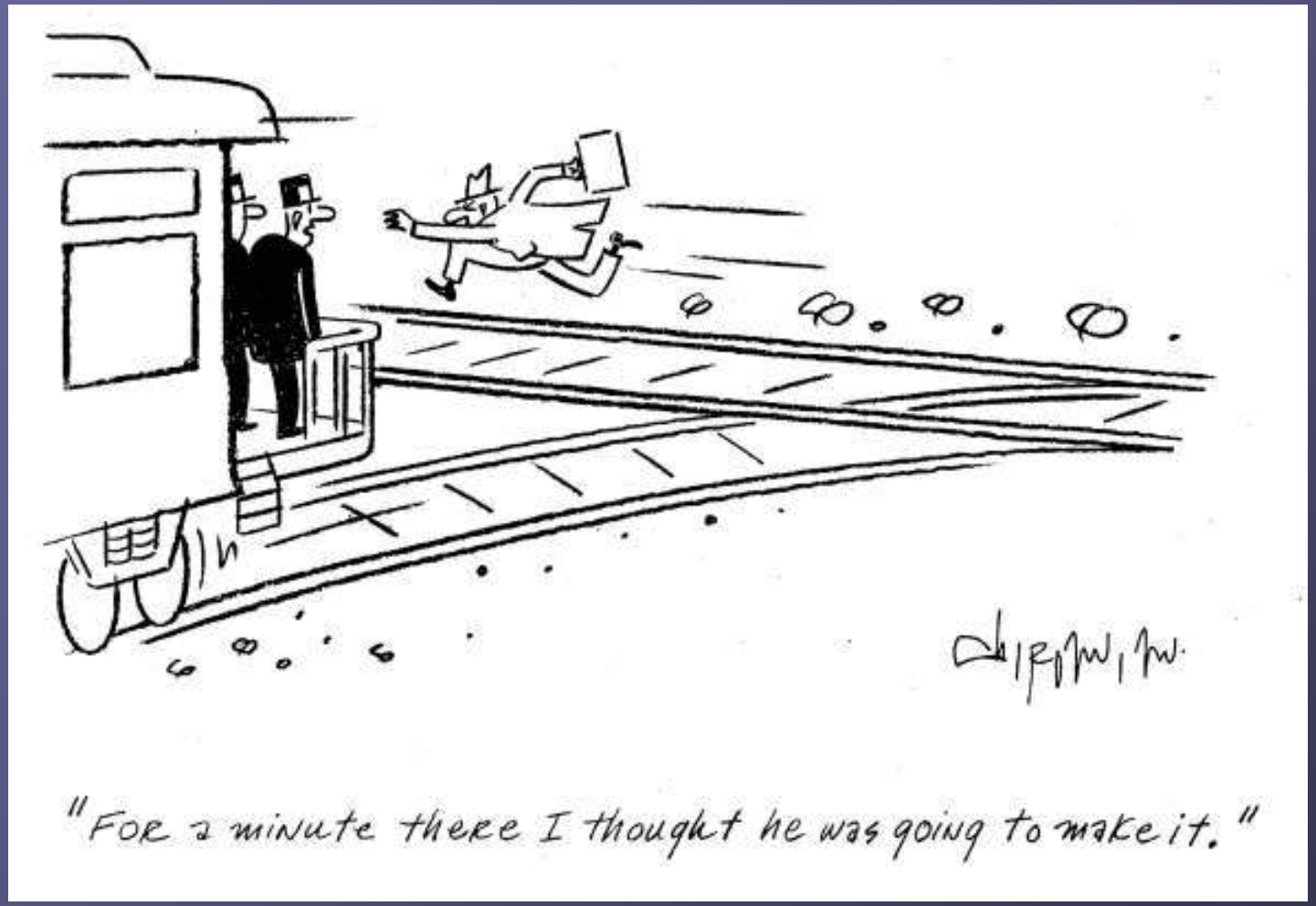
"Better safe than sorry" approach

"In view of the dangers to society that could arise out of the establishment of nanotechnology, and given the uncertainty currently prevailing in scientific circles, the precautionary principle should be applied whatever the difficulties….This is particularly important for individuals whose jobs expose them to nanoparticles on a regular basis."

"Nanotechnology: Small matter, many unknowns" Swiss Reinsurance Co., 2004



- "... reason we are in this mess is because you didn't take it seriously in the first place. You had a **runaway swarm** out there in the desert for what-two weeks? And instead of eradicating it, you played with it. You fooled around ..."



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…with nanotechnology, we still have the chance to make a difference before the train leaves the station